Covid-19 overtakes 1918 Spanish flu as deadliest disease in American history

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By Helen Branswell Sept. 20, 2021

Volunteer nurses from the American Red Cross tend to influenza patients in the Oakland Municipal Auditorium, used as a temporary hospital in 1918. *Edward A. "Doc" Rogers/Library of Congress via AP*

The Covid-19 pandemic has become the deadliest disease event in American history, with a death toll surpassing that of the 1918 Spanish flu.

The Spanish flu was previously the disease event that caused the biggest loss of life in the United States; the Centers for Disease Control and Prevention

estimate that 675,000 Americans died during the 1918 pandemic, in waves of illness that stretched out over roughly two years in this country.

According to STAT's Covid-19 Tracker, Covid deaths stand at more than 675,400.

"In terms of raw numbers of deaths, that's a high number," said Howard Markel, director of the Center for the History of Medicine at the University of Michigan School of Public Health. "And it's higher still than it should have been, frankly."

U.S. deaths make up roughly 14% of the nearly 4.7 million fatalities that have been reported worldwide in this pandemic to date, even though the country's population comprises only about 4.2% of the global population.

"In the U.S., we are among the worst affected in our class of countries — rich countries with an aging population. But other countries in Europe did poorly as well," said Cécile Viboud, an infectious diseases epidemiologist who has done a lot of research into deaths from the 1918 flu.

Whether the Covid pandemic will qualify as the deadliest event in U.S. history is perhaps a question for Civil War historians. The long-accepted toll of the War Between the States was 620,000, which this pandemic has already surpassed. But in 2011, David Hacker, a historian at Binghamton University in New York State, published an article in the journal Civil War History arguing the true number of deaths in the Civil War was more likely around 750,000.

The heavy toll the pandemic has taken in the U.S. is due to the country's inadequate response early on, said Markel. David Morens, a medical historian at the National Institutes of Allergy and Infectious Diseases, agreed.

"I think it's generally known around the world that America didn't do a very good job in the early stages of controlling the pandemic," said Morens, who has also written extensively on the 1918 flu pandemic.

Comparing events that happened more than a century apart has its perils. For instance, the population of the United States in 1918 was a third of what it is now. So as a percentage of the national population, the Spanish flu deaths still has the lead on Covid-19.

Likewise, the mean age of the people who died in 1918 was 28, whereas with Covid, deaths are occurring mainly in the elderly, said Viboud, who works at the National Institutes of Health's Fogerty International Center. In terms of cumulative years of life lost, the Spanish flu's impact thus remains greater.

But modern medicine is far more advanced than what was available in 1918. Now people whose lungs are under attack from Covid can be put on ventilators or extracorporeal membrane oxygenation — ECMO — machines, which pump oxygen into blood when a person's heart and lungs are no longer up to the job. These were not options in 1918.

And for months now, the country has had vaccines that are highly effective at lowering the risk of dying from Covid. Still the fatalities pile up, though at a slower rate than earlier in the pandemic.

"We have no idea what would have been the impact of Covid-19 without interventions," Viboud acknowledged.

The deaths will continue to climb for some time still, Morens noted.

"Remember, we're still counting," he said. "In 1918, the pandemic became not so deadly within two years. We have no idea — I don't and I don't trust anybody who says they do — where this Covid-19 will go."

The global Covid death figure is without doubt an underestimate, but then again, the American tally likely is as well.

"The true deaths from Covid-19 in the United States are probably higher than the actual numbers. But how much higher is a matter of speculation," Morens

said.

There is some work that suggests what a truer figure might be, Viboud said, pointing to a research paper published in the journal eLife in June.

The study, by Ariel Karlinsky, an economist and statistician at Hebrew University in Jerusalem, and Dmitry Kobak, of the Institute for Ophthalmic Research at the University of Tübingen in Germany, actually attempted to estimate a more accurate picture of Covid deaths in 103 countries. Their calculations were based on looking at what is known as excess mortality, the differences between the number of deaths reported since the start of the pandemic and the annual average mortality figures for the years 2015 through 2019 in each of the countries studied.

Some countries have actually had fewer deaths — negative excess mortality — during the pandemic. One such country is New Zealand, which has managed in the main to keep Covid from spreading by using stringent border controls. New Zealand reported 1,900 fewer deaths than normal during the pandemic, the Karlinsky and Kobak paper reported, attributing the lower number of deaths to the fact that viruses like influenza haven't circulated to normal degrees during the pandemic.

Their work estimated that the true Covid death toll in the United States is probably 10% higher than the declared number of lives lost to the disease in the country. That would place the Covid deaths in America in the ballpark of 741,000.

In rivaling the Spanish flu, the Covid-19 pandemic has given medical historians a new lesson to teach, said Markel, who wrote about that fact last month in The Atlantic.

"The truth is we have no historical precedent for the moment we're in now," he wrote. "We need to stop thinking back to 1918 as a guide for how to act in

the present and to start thinking forward from 2021 as a guide to how to act in the future."

In his interview with STAT, Markel recalled that during a briefing he gave to former President Barack Obama about the 1918 pandemic — he was president during the 2009 H1N1 pandemic — Obama noted that 1918 was a long time ago. That's the problem with disease outbreaks that are 100-year events; they are so rare that the lessons one can take from them may seem out of date when they are next needed.

"We finally now have a modern pandemic," said Markel. "In modern times with modern vaccines and so on. So to me, this is the one I'm going to be teaching my medical students and public health students."

This story has been updated.

About the Author

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Helen covers issues broadly related to infectious diseases, including outbreaks, preparedness, research, and vaccine development.

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15 Comments

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COVID-19 Public Health and Medical Emergency Declarations and Waivers

Emergency Declarations

- January 7, 2021: Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic
- October 2, 2020: Renewal of the Determination that a Public Health Emergency Exists as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic
- July 23, 2020: Renewal of the Determination that a Public Health Emergency Exists as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic
- April 21, 2020: Renewal of the Determination that a Public Health Emergency Exists as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) (formerly called 2019 Novel Coronavirus (2019-nCoV)) Pandemic
- March 13, 2020: Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak
- January 31, 2020: Public Health Emergency Declaration

1135 Waiver

- March 13, 2020: Waiver of Modification of Requirements Under Section 1135 of the Social Security Act as a Result of the of the Consequences of the 2019 Novel Coronavirus

PREP Act Declaration

Declaration and Amendments to the PREP Act

- Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 (March 17, 2020)
- First Amendment to Declaration under the PREP Act for Medical Countermeasures against COVID-19 (April 15, 2020)
- Second Amendment to Declaration under the PREP Act for Medical Countermeasures against COVID-19 (June 8, 2020)
- Third Amendment to Declaration under the PREP Act for Medical Countermeasures Against COVID–19 (August 24, 2020)
- Fourth Amendment to Declaration under the PREP Act for Medical Countermeasures Against COVID–19 (December 3, 2020)
- Fifth Amendment to Declaration under the PREP Act for Medical Countermeasures Against COVID–19 (January 28, 2021)
- Sixth Amendment to Declaration under the PREP Act for Medical Countermeasures Against COVID–19 (February 16, 2021)
- Technical Correction to Fifth and Sixth Amendments to Declaration under the PREP Act for Medical Countermeasures Against COVID-19 (February 22, 2021)
- Seventh Amendment to Declaration under the PREP Act for Medical Countermeasures Against COVID–19 (March 11, 2021)

Advisory Opinions of the General Counsel on the PREP Act

- First Advisory Opinion on the PREP Act Declaration (May 19, 2020)
- Second Advisory Opinion on the PREP Act Declaration (May 19, 2020)
- Third Advisory Opinion on the PREP Act Declaration (October 23, 2020)
- Fourth Advisory Opinion on the PREP Act Declaration (October 23, 2020)
- Fifth Advisory Opinion on the PREP Act Declaration (January 8, 2021)
- Sixth Advisory Opinion on the PREP Act Declaration (January 12, 2021)

COVID-19: Coronavirus Disease 2019

- BARDA's Novel Coronavirus Medical Countermeasure Portfolio
- Working with BARDA on COVID-19 Medical Countermeasures
- Strategic National Stockpile
- Healthcare Provider Resources from ASPR TRACIE
- HPP and Health Care System Preparedness and Response
- Emergency Declarations and Waivers
- Mental and Behavioral Health
- Volunteering and Community Service
- Federal Nutrition Programs for At-Risk Individuals
- Online Training Webinars and Peer-to-Peer Sessions

HHS Guidance on the PREP Act

- Guidance for National Guard Personnel Regarding COVID-19 Vaccines and Immunity under the PREP Act (December 18, 2020)
- Guidance for Department of Defense Personnel, Contractors, and Volunteers Regarding COVID-19 Vaccines and Immunity under the PREP Act (February 2, 2021)
- PREP Act Authorization for Pharmacies Distributing and Administering Certain Covered Countermeasures (October 29, 2020)
- Guidance for PREP Act Coverage for Qualified Pharmacy Technicians and State-Authorized Pharmacy Interns for Childhood Vaccines, COVID-19 Vaccines, and COVID-19 Testing (October 20, 2020)
- Guidance for Licensed Pharmacists and Pharmacy Interns Regarding COVID-19 Vaccines and Immunity under the PREP Act (September 3, 2020)
- Guidance for Licensed Pharmacists, COVID-19 Testing, and Immunity under the PREP Act (April 8. 2020)
- Guidance for PREP Act Coverage for COVID-19 Screening Tests at Nursing Homes, Assisted-Living Facilities, Long-Term-Care Facilities, and other Congregate Facilities (August 31, 2020)

HIPAA

- March 2020: Limited Waiver of HIPAA Sanctions and Penalties During a Nationwide Public Health Emergency

Administrative Relief

- March 19, 2020: Administrative Relief for Recipients and Applicants of Federal Financial Assistance Directly impacted by the Novel Coronavirus (COVID-19) due do Loss of Operations

This page last reviewed: April 16, 2021

Public Health Emergency Declarations

The Secretary of the Department of Health and Human Services (HHS) may, under section 319 of the Public Health Service (PHS) Act determine that: a) a disease or disorder presents a public health emergency; or b) that a public health emergency, including significant outbreaks of infectious disease or bioterrorist attacks, otherwise exists. Learn More >>

Title	Disaster Type	State/Territory	Signed Date
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic	COVID-19	National	October 15, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of the Opioid Crisis	Opioid Crisis	National	October 6, 2021
Determination That A Public Health Emergency Exists as the Result of the Consequences of the Remnants of Hurricane Ida in New York and New Jersey	Hurricane	New York and New Jersey	September 3, 2021
Determination That A Public Health Emergency Exists as the Result of the Consequences of Hurricane Ida in Louisiana and Mississippi	Hurricane	Louisiana and Mississippi	August 30, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic	COVID-19	National	July 19, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of the Opioid Crisis	Opioid Crisis	National	July 7, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic	COVID-19	National	April 15, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of the Opioid Crisis	Opioid Crisis	National	April 7, 2021
Determination that a Public Health Emergency Exists in the State of Texas as the Result of the	Winter Storm	Texas	February 17, 2021

More Emergency and Response Information
- Declarations of a Public Health Emergency
- Public Health Emergency Determinations to Support an Emergency Use Authorization
- Section 1135 Waivers
- Emergency Use Authorizations

Public Health Emergency
- Stay Connected
- Emergency Response Guide
- Natural Disasters
- Bioterrorism & Mass Casualty
- Outbreaks and Pandemics
- Public Health Response
- Sustained Recovery

Winter Storm			
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of the Opioid Crisis	Opioid Crisis	National	January 7, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic	COVID-19	National	January 7, 2021
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	October 7, 2020
Renewal of the Determination that a Public Health Emergency Exists as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic	COVID-19	National	October 2, 2020
Determination that a Public Health Emergency Exists in the State of Oregon as the Consequences of Wildfires	Wildfire	Oregon	September 16, 2020
Determination that a Public Health Emergency Exists in the State of Louisiana and the State of Texas as a Result of Hurricane Laura	Hurricane	Louisiana	August 26, 2020
Determination that a Public Health Emergency Exists in the State of California as a Result of Wildfires	Wildfire	California	August 26, 2020
Renewal of the Determination that a Public Health Emergency Exists as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) Pandemic	COVID-19	National	July 23, 2020
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	July 6, 2020
Renewal of the Determination that a Public Health Emergency Exists as the Result of the Continued Consequences of Coronavirus Disease 2019 (COVID-19) (formerly called 2019 Novel Coronavirus (2019-nCoV)) Pandemic	COVID-19	National	April 21, 2020
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	April 2, 2020
Determination that a Public Health Emergency Exists Nationwide as the Result of the 2019 Novel Coronavirus	COVID-19	National	January 31, 2020
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	January 24, 2020
Determination that a Public Health Emergency	Earthquake	Commonwealth of	January 8, 2020

Exists as a Result of the Consequences of Earthquakes on the Commonwealth of Puerto Rico		Puerto Rico	
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	October 16, 2019
Determination that a Public Health Emergency Exists in the State of North Carolina as the Result of Hurricane Dorian	Hurricane	North Carolina	September 4, 2019
Determination that a Public Health Emergency Exists in the State of Georgia as the Result of Hurricane Dorian	Hurricane	Georgia	September 2, 2019
Determination that a Public Health Emergency Exists in the State of South Carolina as the Result of Hurricane Dorian	Hurricane	South Carolina	September 2, 2019
Determination that a Public Health Emergency Exists in the State of Florida as the Result of Hurricane Dorian	Hurricane	Florida	August 30, 2019
Determination that a Public Health Emergency Exists in the Commonwealth of Puerto Rico as the Result of Tropical Storm Dorian	Tropical Storm	Commonwealth of Puerto Rico	August 28, 2019
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	July 17, 2019
Determination that a Public Health Emergency Exists in Louisiana as a Result of Tropical Storm Barry	Tropical Storm	Louisiana	July 12, 2019
Renewal of the Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	April 19, 2019
Renewal of the Determination that a Public Health Emergency Exists in California as a Result of the Wildfires	Wildfire	California	January 30, 2019
Renewal of Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	January 17, 2019
Renewal of Determination that a Public Health Emergency Exists in the Commonwealth of the Mariana Islands as the Result of Typhoon Yutu	Typhoon	Commonwealth of the Mariana Islands	January 17, 2019
Determination that a Public Health Emergency Exists in Alaska as a Result of the Earthquake	Earthquake	Alaska	December 3, 2018
November 13, 2018: Determination that a Public Health Emergency Exists in California as a Result of the Wildfires	Wildfire	California	November 13, 2018
Determination that a Public Health Emergency Exists in the Commonwealth of the Mariana Islands as the Result of Typhoon Yutu	Typhoon	Commonwealth of the Mariana Islands	October 25, 2018

Renewal of Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	October 18, 2018
Determination that a Public Health Emergency Exists in Georgia as the Result of Hurricane Michael	Hurricane	Georgia	October 11, 2018
Determination that a Public Health Emergency Exists in Florida as the Result of Hurricane Michael	Hurricane	Florida	October 9, 2018
Determination that a Public Health Emergency Exists in the Commonwealth of Virginia as the Result of Hurricane Florence	Hurricane	Commonwealth of Virginia	September 12, 2018
Renewal of Determination that a Public Health Emergency Exists in the Territory of the U.S. Virgin Islands as a Result of Hurricane Maria	Hurricane	Territory of the U.S. Virgin Islands	September 11, 2018
Determination that a Public Health Emergency Exists in North Carolina and South Carolina as the Result of Hurricane Florence	Hurricane	North Carolina, South Carolina	September 11, 2018
Renewal of Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	July 23, 2018
Renewal of Determination that a Public Health Emergency Exists in the Territory of the U.S. Virgin Islands as a Result of Hurricane Maria	Hurricane	Territory of the U.S. Virgin Islands	June 12, 2018
Renewal of Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	April 20, 2018
Renewal of Determination that a Public Health Emergency Exists in the Commonwealth of Puerto Rico as a Result of Hurricane Maria	Hurricane	Commonwealth of Puerto Rico	March 16, 2018
Renewal of Determination that a Public Health Emergency Exists in the Territory of the U.S. Virgin Islands as a Result of Hurricane Maria	Hurricane	Territory of the U.S. Virgin Islands	March 15, 2018
Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	January 19, 2018
Determination that a Public Health Emergency Exists in the Territory of the U.S. Virgin Islands and the Commonwealth of Puerto Rico as the Result of Hurricane Maria	Hurricane	Territory of the U.S. Virgin Island Commonwealth of Puerto Rico	December 11, 2017
Determination that a Public Health Emergency Exists Nationwide as the Result of the Opioid Crisis	Opioid Crisis	National	October 26, 2017
Determination that a Public Health Emergency Exists in California as the Result of Wildfires	Wildfire	California	October 15, 2017
Determination that a Public Health Emergency Exists in Alabama as the Result of Hurricane	Hurricane	Alabama	October 8, 2017

Nate			
Determination that a Public Health Emergency Exists in Florida as the Result of Hurricane Nate	Hurricane	Florida	October 8, 2017
Determination that a Public Health Emergency Exists in Mississippi as the Result of Hurricane Nate	Hurricane	Mississippi	October 8, 2017
Determination that a Public Health Emergency Exists in Louisiana as the Result of Hurricane Nate	Hurricane	Louisiana	October 8, 2017
Determination that a Public Health Emergency Exists in the Territory of the U.S. Virgin Islands and the Commonwealth of Puerto Rico as the Result of Hurricane Maria	Hurricane	Territory of the U.S. Virgin Islands Commonwealth of Puerto Rico	September 19, 2017
Determination that a Public Health Emergency Exists in South Carolina as the Result of Hurricane Irma	Hurricane	South Carolina	September 8, 2017
Determination that a Public Health Emergency Exists in Georgia as the Result of Hurricane Irma	Hurricane	Georgia	September 8, 2017
Determination that a Public Health Emergency Exists in Florida as the Result of Hurricane Irma	Hurricane	Florida	September 8, 2017
Determination that a Public Health Emergency Exists in Florida as the Result of Hurricane Irma	Hurricane	Florida	September 7, 2017
Determination that a Public Health Emergency Exists in the Commonwealth of Puerto Rico and the Territory of the U.S. Virgin Islands as the Result of Hurricane Irma	Hurricane	Commonwealth of Puerto Rico Territory of the U.S. Virgin Islands	September 6, 2017
Determination that a Public Health Emergency Exists in Louisiana as the Result of Hurricane Harvey	Hurricane	Louisiana	August 28, 2017
Determination that a Public Health Emergency Exists in Texas as the Result of Hurricane Harvey	Hurricane	Texas	August 26, 2017
Renewal of Determination that a Public Health Emergency Exists as a Consequence of the Zika Virus Outbreak	Zika Virus Outbreak	National	April 28, 2017
Renewal of Determination that a Public Health Emergency Exists as a Consequence of the Zika Virus Outbreak	Zika Virus Outbreak	National	January 31, 2017
Renewal of Determination that a Public Health Emergency Exists as a Consequence of the Zika Virus Outbreak	Zika Virus Outbreak	National	November 4, 2016
Determination that a Public Health Emergency Exists in Puerto Rico as a Consequence of the Zika Virus Outbreak	Zika Virus Outbreak	Puerto Rico	August 12, 2016

Determination that a Public Health Emergency Exists in New York as a Consequence of Hurricane Sandy (Renewal)	Hurricane	New York	January 25, 2013
Determination that a Public Health Emergency Exists in New Jersey as a Consequence of Hurricane Sandy	Hurricane	New Jersey	November 1, 2012
Determination that a Public Health Emergency Exists in New York as a Consequence of Hurricane Sandy	Hurricane	New York	October 31, 2012
Determination that a Public Health Emergency Exists in Missouri as a Consequence of Severe Storms and Tornadoes in the Area (Renewal)	Severe Storm Tornado	Missouri	February 15, 2012
Determination That a Public Health Emergency Exists in the State of New York (Renewal)		New York	December 22, 2011
Determination that a Public Health Emergency Exists in Missouri as a Consequence of Severe Storms and Tornadoes in the Area (Renewal)	Severe Storm Tornado	Missouri	November 18, 2011
Determination that a Public Health Emergency Exists as a Consequence of the Remnants of Tropical Storm Lee in the State of New York	Tropical Storm	New York	September 24, 2011
Determination that a Public Health Emergency Exists in Missouri as a Consequence of Severe Storms and Tornadoes in the Area (Renewal)	Severe Storm Tornado	Missouri	August 19, 2011
Determination that a Public Health Emergency Exists in Missouri as a Consequence of Severe Storms and Tornadoes in the Area	Severe Storm Tornado	Missouri	May 23, 2011
Flooding in North Dakota: Determination That a Public Health Emergency Exists	Flood	North Dakota	April 8, 2011
2009 H1N1 Flu Outbreak: Determination that a Public Health Emergency Exists (Renewal)	H1N1 Flu Outbreak	National	March 22, 2010
Flooding in North Dakota: Determination That A Public Health Emergency Exists	Flood	North Dakota	March 18, 2010
2009 H1N1 Flu Outbreak: Determination that a Public Health Emergency Exists (Renewal)	H1N1 Flu Outbreak	National	December 28, 2009
2009 H1N1 Flu Outbreak: Determination that a Public Health Emergency Exists (Renewal)	H1N1 Flu Outbreak	National	October 1, 2009
2009 H1N1 Flu Outbreak: Determination that a Public Health Emergency Exists (Renewal)	H1N1 Flu Outbreak	National	July 24, 2009
2009 H1N1 Flu Outbreak: Determination that a Public Health Emergency Exists	H1N1 Flu Outbreak	National	April 26, 2009
Determination that a Public Health Emergency Exists as a Consequence of Severe Flooding in North Dakota	Flood	North Dakota	March 25, 2009
Determination that a Public Health Emergency Exists as a Consequence of Severe Flooding in	Flood	Minnesota	March 27, 2009

Minnesota			
The 56th Presidential Inauguration	Presidential Inauguration		January 16, 2009
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Ike in the State of Louisiana	Hurricane	Louisiana	September 13, 2008
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Ike in the State of Texas	Hurricane	Texas	September 11, 2008
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Gustav in the State of Louisiana	Hurricane	Louisiana	August 31, 2008
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Gustav in the State of Texas	Hurricane	Texas	August 31, 2008
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Gustav in the State of Alabama	Hurricane	Alabama	August 31, 2008
Determination that a Public Health Emergency Exists as a Consequence of Severe Flooding in Iowa	Flood	Iowa	June 14, 2008
Determination that a Public Health Emergency Exists as a Consequence of Severe Flooding in Indiana	Flood	Indiana	June 14, 2008
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Dean in the State of Texas	Hurricane	Texas	August 19, 2007
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Rita in the State of Texas	Hurricane	Texas	September 23, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Dean in the State of Louisiana	Hurricane	Louisiana	September 23, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Texas	Hurricane	Texas	September 4, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Arkansas	Hurricane	Arkansas	September 7, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Colorado	Hurricane	Colorado	September 7, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Georgia	Hurricane	Georgia	September 7, 2005
Determination that a Public Health Emergency	Hurricane	North Carolina	September 7, 2005

Exists as a Consequence of Hurricane Katrina in the State of North Carolina			
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Oklahoma	Hurricane	Oklahoma	September 7, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Tennessee	Hurricane	Tennessee	September 7, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of West Virginia	Hurricane	West Virginia	September 7, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Utah	Hurricane	Utah	September 7, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Florida	Hurricane	Florida	August 31, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Alabama	Hurricane	Alabama	August 31, 2005
Determination that a Public Health Emergency Exists as a Consequence of Hurricane Katrina in the State of Mississippi	Hurricane	Mississippi	August 31, 2005

This page last reviewed: October 15, 2021

CDC Centers for Disease Control and Prevention

COVID-19 Vaccination Coverage and Vaccine Confidence

COVIDVaxView

User Quick Guide | Download Data Table | Back to COVIDVaxView main page

Vaccination and Intent Profile Table - National

Data Collection Period: August 29 - September 25

Indicators / Groups	All: All adults age 18+ years	Vaccination Coverage: Unvaccinated	Vaccination Uptake and Intention: Vaccinated (≥1 dose)	Definitely will get vaccinated	Probably will get vaccinated or are unsure	Probably or definitely will not get vaccinated
Demographics						
Sex						
Female	51.6	47.1	53.1	48.6	48.3	46.0
Male	48.4	52.9	46.9	51.4	51.7	54.0
Age						
18 – 49 years	54.3	74.6	47.7	77.6	75.5	73.5
50 – 64 years	24.3	18.5	26.2	15.9	18.4	19.0
65+ years	21.4	6.9	26.1	6.5	6.2	7.4
Race/Ethnicity						
Hispanic	17.2	17.8	17.0	25.5	21.4	14.3
White, non-Hispanic	62.2	61.1	62.6	49.0	53.6	67.8

Page last reviewed: September 23, 2021

VIEWPOINT

COVID-19 Vaccination of Health Care Personnel as a Condition of Employment

A Logical Addition to Institutional Safety Programs

Thomas R. Talbot, MD, MPH
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Viewpoint page 25

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The consequences of the SARS-CoV-2 pandemic have been far-reaching, particularly among health care personnel (HCP) and within health care settings. HCP have been directly affected, sustaining occupationally acquired COVID-19 infections, and indirectly through a substantial alteration in health care delivery. With the advent of highly effective and safe SARS-CoV-2 vaccines, case rates and hospitalization rates are declining, and the promise of a return to some semblance of pre–COVID-19 health care is growing. Recently, several medical centers have announced a requirement for SARS-CoV-2 vaccination of all HCP (allowing for medical and religious exemptions), and the impending licensure of the mRNA SARS-CoV-2 vaccines (following the previous Emergency Use Authorization [EUA]) will move many other centers to consider a similar policy. A recent outbreak in a skilled nursing facility attributed to an unvaccinated HCP member clearly illustrates the risk unvaccinated HCP can pose to their patients and other HCP.[1]

> Health care systems should learn from the decisions on influenza vaccination requirements for HCP [health care personnel] in drafting SARS-CoV-2 vaccination policies for HCP.

The recognition of HCP vaccination as an essential component of patient and HCP safety programs emerged in the mid-2000s with a focus on influenza vaccination. Prior to the 2009-2010 influenza season, despite increased awareness of the importance of HCP influenza vaccination and large-scale, resource-intensive voluntary vaccination campaigns, vaccination rates remained very low. While HCP influenza vaccination was first recommended by the Advisory Committee on Immunization Practices in 1978, innovative, patient safety–focused programs at hospitals like Virginia Mason Medical Center paved the way for stronger expectations surrounding HCP vaccination.[2] The success at these institutions, professional society endorsements of influenza vaccination as a condition of employment policies, and the addition of HCP influenza vaccination as a publicly reported quality measure were associated with increases in vaccination rates from around 45% to nearly 80%, with higher rates among acute care facilities, physicians, and nursing personnel.[3] During the 2019-2020 season, the percentage of hospital-based HCP who reported working under an employer influenza vaccination requirement reached 72.1%.[3] Very few HCP have had their employment terminated due to policy refusal, particularly considering the thousands encompassed by these policies.

Mandatory influenza vaccination programs for HCP have been associated with high vaccination rates and a significant decrease in HCP absenteeism and health care–associated influenza among hospitalized patients.[4] The importance of mandatory influenza vaccination for HCP is best reflected by the decision of the National Patient Safety Foundation board to establish the inaugural "must do" list for all HCP to ensure patient safety: hand washing and HCP influenza vaccination.[5]

With the advent of highly effective SARS-CoV-2 vaccines, the HCP vaccination discussion has turned their direction. Health care systems should learn from the decisions on influenza vaccination requirements for HCP in drafting SARS-CoV-2 vaccination policies for HCP.[4] The rationale to move from an HCP voluntary program to a condition of employment policy for a vaccine-preventable infection centers on several important questions:

Do HCP become infected with the pathogen? Are HCP at an increased risk for infection due to their occupation? HCP clearly become infected with SARS-CoV-2, with many experiencing severe outcomes, including some deaths. Whether HCP are at higher risk for SARS-CoV-2 infection is less clear. Studies early in the pandemic reflected a higher infection risk in this population but that risk may have been mitigated by increased availability and use of universal personal protective equipment.

Can HCP have asymptomatic infection with the pathogen? Do these HCP still spread the pathogen to others? As with the general population, the proportion of SARS-CoV-2 infections among HCP that are asymptomatic is substantial. These individuals often have a high quantity of virus in their upper airways and have accounted for many instances of transmission.[6]

Is there a vaccine that is safe and effective in preventing infection? One of the true scientific triumphs of the COVID-19 pandemic has been the development of safe and highly effective vaccines against SARS-CoV-2. With widespread SARS-CoV-2 vaccination across the world, similar effectiveness has been noted. Reassuringly, the safety profile of the vaccines has also remained excellent.

Does vaccination affect pathogen transmission? While not specifically studied in the clinical trials, mounting evidence suggests that the vaccines are associated

with decreased asymptomatic infections and transmission (as measured in household contact studies) of SARS-CoV-2.[7] A lower risk of COVID-19 infection was noted among household contacts of vaccinated HCP in the United Kingdom compared with household members of unvaccinated HCPs (absolute rates, 5.93 vs 9.40 per 100 person-years; hazard ratio, 0.70 [95% CI, 0.63-0.78]),[8] whereas a study examining infection rates in 223 discrete communities in Israel identified a strong negative correlation between community rates of vaccination and a later decline in infections among a cohort of unvaccinated persons younger than 16 years old.[9]

Do HCP have frequent contact with individuals who cannot mount a robust immune response to vaccination (and, therefore, rely on others to reduce exposure)? HCP, by nature of their occupation, have direct contact with patients (and other HCP) who will not be as protected by their own SARS-CoV-2 vaccination. Data are emerging of lower, if not negligible, immune responses postvaccination in certain populations (eg, recipients of solid organ transplants). Even HCP without direct contact with these immunocompromised persons will have contact with HCP who do, and the efficient spread of a respiratory pathogen makes anyone working in a health care facility a potential vector to the most vulnerable patients.

Do voluntary HCP vaccination programs attain high enough coverage to prevent pathogen transmission? Uptake of SARS-CoV-2 vaccination among HCP, while greater than the general public, is below the level necessary to prevent introduction and spread of the virus in health care settings. While population-level COVID-19 vaccination rates among HCP are not widely available, in one survey from early March 2021, only 52% of 1327 HCP reported receipt of at least 1 dose of a COVID-19 vaccine.[10]

Examination of these key questions drove the implementation of influenza vaccination as a condition of employment policies for HCP. Examining them through the lens of COVID-19 finds that the arguments for SARS-CoV-2 vaccination as a condition of HCP employment are even stronger.

As health care facility leaders evaluate whether to include SARS-CoV-2 vaccination within such policies for HCP, several important logistic concerns should be noted. First, whether any vaccine approved under an EUA by the US Food and Drug Administration can actually be mandated is unclear. Legal scholars have cited the language in the EUA portion of the Federal Food, Drug, and Cosmetic Act around an option to "refuse" a product approved under an EUA but noted mention of "consequences" of such refusal. Leaders of health care facilities have expressed a desire to place a hold on any COVID-19 vaccination requirement for HCP while the vaccines are under EUA approval. With the impending full licensure of the mRNA COVID-19 vaccines, however, this concern will soon become moot.

Second, any such program should make allowances for individuals who cannot be vaccinated. While the currently approved vaccines have very few medical contraindications, some HCP may develop allergic reactions to the first dose of an mRNA vaccine and may not be able to receive the second dose necessary for full immunity. Such HCP could opt for other types of COVID-19 vaccines (such as a viral vector vaccine), so even in those instances, HCP unable to take any COVID-19 vaccine due to a medical contraindication should be rare. Exemptions to vaccination on religious or personal beliefs are more complicated. With the example of influenza, most organized religions endorse receipt of vaccines, and allowance of such exemptions can increase the risk of SARS-CoV-2 introduction into the health care setting. Nonetheless, providing a venue for such concerns to be thoughtfully reviewed can be important for acceptance of these policies.

Third, as with many influenza vaccination policies for HCP, alternative approaches for HCP who are unable or refuse to be vaccinated should be included. These may be a requirement for use of infection prevention measures to protect patients and other HCP (eg, masking when working in the health care facility) or added assessments of asymptomatic infection among unvaccinated HCP (eg, periodic testing for asymptomatic infection) when SARS-CoV-2 is circulating. Unlike influenza, however, COVID-19 has yet to exhibit seasonal trends that would allow clear delineation when such interventions for unvaccinated HCP should be in place.

As the SARS-CoV-2 vaccines move closer to full licensure and the data on their excellent effectiveness against both symptomatic and asymptomatic COVID-19 infection emerge, the question of whether to implement a SARS-CoV-2 vaccination policy for HCP as a condition of employment is becoming clearer. HCP should not inadvertently spread contagious infections like measles and influenza to their patients and other HCP. The time is coming to add COVID-19 to that list.

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Conflict of Interest Disclosures: None reported.

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Centers for Disease Control and Prevention

COVID-19

COVID-19 Vaccination Toolkits

Updated Apr. 8, 2021 Print

Get audience-specific toolkits for healthcare teams and community administrators.

Health Departments and Public Health Partner Vaccination Toolkit

For health departments and public health partners

Help educate communities and promote the importance COVID-19 vaccination.

Vaccination Communication Toolkit

For Medical Centers, Clinics, Pharmacies, and Clinicians

Build confidence about COVID-19 vaccination among your healthcare teams and other staff.

Recipient Education Toolkit

For Healthcare Professionals and Pharmacists

Educate vaccine recipients about the importance of COVID-19 vaccination.

Essential Worker Vaccination Toolkit

For Employers of Essential Workers

Help plan for and encourage COVID-19 vaccination in the workplace.

Community-Based Organization (CBO) Vaccination Toolkit

For Staff of Organizations Serving Communities

Educate communities about the benefits of COVID-19 vaccination, and address common questions and concerns.

School Settings and Childcare Programs Toolkit

For school districts, administrators, teachers, school staff, and other education and childcare professionals

Share messages about COVID-19 vaccines, promote confidence in the decision to get vaccinated, and engage school and childcare staff.

Find social media ready COVID-19 vaccines content so you can put together Facebook, Twitter, and Instagram posts.

Last Updated Apr. 8, 2021

Centers for Disease Control and Prevention

COVID-19

COVID-19 Vaccine Booster Shots

Updated Oct. 27, 2021

Some COVID-19 Vaccine Recipients Can Get Booster Shots

- People 65 years and older, 50–64 years with underlying medical conditions, or 18 years and older who live in long-term care settings should receive a booster shot.
- People 18 years and older should receive a booster shot at least 2 months after receiving their Johnson & Johnson/Janssen COVID-19 vaccine.

IF YOU RECEIVED

Pfizer-BioNTech or Moderna

You are eligible for a booster if you are:

- 65 years or older
- Age 18+ who live in long-term care settings
- Age 18+ who have underlying medical conditions
- Age 18+ who work or live in high-risk settings

When to get a booster:
At least 6 months after your second shot

Which booster should you get?
Any of the COVID-19 vaccines authorized in the United States

IF YOU RECEIVED

Johnson & Johnson's Janssen

You are eligible for a booster if you are:
18 years or older

When to get a booster:
At least 2 months after your shot

Which booster should you get?
Any of the COVID-19 vaccines authorized in the United States

Choosing Your COVID-19 Booster Shot

You may choose which COVID-19 vaccine you receive as a booster shot. Some people may have a preference for the vaccine type that they originally received, and others may prefer to get a different booster. CDC's recommendations now allow for this type of mix and match dosing for booster shots.

Learn how you can find a COVID-19 vaccine near you.

IF YOU RECEIVED

Pfizer-BioNTech or Moderna COVID-19 Vaccine

Older adults age 65 years and older

Older adults ages 65 years and older

People ages 65 years and older **should** get a booster shot. The risk of severe illness from COVID-19 increases with age and can also increase for adults of any age with underlying medical conditions.

Long-term care setting residents ages 18 years and older

Residents ages 18 years and older of long-term care settings **should** get a booster shot. Because residents in long-term care settings live closely together in group settings and are often older adults with underlying medical conditions, they are at increased risk of infection and severe illness from COVID-19.

People with underlying medical conditions ages 50–64 years

People ages 50–64 years with underlying medical conditions **should** get a booster shot. The risk of severe illness from COVID-19 increases with age and can also increase for adults of any age with underlying medical conditions.

People with underlying medical conditions ages 18–49 years

People ages 18–49 years with underlying medical conditions **may** get a booster shot based on their individual risks and benefits. The risk of severe illness from COVID-19 can increase for adults of any age with underlying medical conditions. This recommendation may change in the future as more data become available.

People who work or live in high-risk settings ages 18–64 years

People ages 18–64 years at increased risk for COVID-19 exposure and transmission because of occupational or institutional setting **may** get a booster shot based on their individual risks and benefits. Adults who work or reside in certain settings (e.g., health care, schools, correctional facilities, homeless shelters) may be at increased risk of being exposed to COVID-19, which could be spreading where they work or reside. That risk can vary across settings and based on how much COVID-19 is spreading in a community. This recommendation may change in the future as more data become available.

Examples of workers who may get COVID-19 booster shots: [1]

- First responders (e.g., healthcare workers, firefighters, police, congregate care staff)
- Education staff (e.g., teachers, support staff, daycare workers)
- Food and agriculture workers
- Manufacturing workers
- Corrections workers
- U.S. Postal Service workers
- Public transit workers
- Grocery store workers

[1] List could be updated in the future.

IF YOU RECEIVED

J&J/Janssen COVID-19 Vaccine

People ages 18 years and older who received a J&J/Janssen COVID-19 vaccine at least 2 months ago **should** get a booster shot. The J&J/Janssen COVID-19 vaccine has lower vaccine effectiveness over time compared to mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna).

Your Vaccination Card and Booster Shots

At your first vaccination appointment, you should have received a CDC COVID-19 Vaccination Record Card that tells you what COVID-19 vaccine you received, the date you received it, and where you received it. Bring this vaccination card to your booster shot vaccination appointment.

If you did not receive a CDC COVID-19 Vaccination Record Card at your first appointment, contact the vaccination site where

you got your first shot or your state health department to find out how you can get a card.

Frequently Asked Questions

Are booster shots the same formulation as existing vaccines?

Yes. COVID-19 booster shots are the same formulation as the current COVID-19 vaccines. However, in the case of the Moderna COVID-19 vaccine booster shot, it is half the dose of the vaccine people get for their initial series.

If we need a booster shot, are the vaccines working?

Yes. COVID-19 vaccines are working well to prevent severe illness, hospitalization, and death, even against the widely circulating Delta variant. However, public health experts are starting to see reduced protection, especially among certain populations, against mild and moderate disease.

What are the risks to getting a booster shot?

So far, reactions reported [707 KB, 24 pages] after getting a booster shot were similar to that of the 2-shot or single-dose initial series. Fever, headache, fatigue and pain at the injection site were the most commonly reported side effects, and overall, most side effects were mild to moderate. However, as with the 2-shot or single-dose initial series, serious side effects are rare, but may occur.

Am I still considered “fully vaccinated” if I don’t get a booster shot?

Yes. Everyone is still considered fully vaccinated two weeks after their second dose in a 2-shot series, such as the Pfizer-BioNTech or Moderna vaccines, or two weeks after a single-dose vaccine, such as the J&J/Janssen vaccine.

When can I get a COVID-19 booster shot if I am NOT in one of the recommended groups?

Additional populations may be recommended to receive a booster shot as more data become available. The COVID-19 vaccines approved and authorized in the United States continue to be effective at reducing risk of severe disease, hospitalization, and death. Experts are looking at all available data to understand how well the vaccines are working for different populations. This includes looking at how new variants, like Delta, affect vaccine effectiveness.

Data Supporting Need for a Booster Shot

Studies show after getting vaccinated against COVID-19, protection against the virus and the ability to prevent infection with the Delta variant may decrease over time.

Although COVID-19 vaccination for adults ages 65 years and older remains effective in preventing severe disease, recent data [5 MB, 88 pages] suggest vaccination is less effective at preventing infection or milder illness with symptoms over time.

- Emerging evidence also shows that among healthcare and other frontline workers, vaccine effectiveness against COVID-19 infections is also decreasing over time.
- This lower effectiveness is likely due to the combination of decreasing protection as time passes since getting vaccinated, as well as the greater infectiousness of the Delta variant.

Data from small clinical trials show that a Pfizer-BioNTech or Moderna **booster shot increased the immune response** in trial participants who finished their initial series 6 months earlier. A similar clinical trial showed that a J&J/Janssen booster shot also **increased the immune response** in participants who completed their single-dose vaccine at least 2 months earlier. With an increased immune response, people should have improved protection against COVID-19, including the Delta variant.

Related Pages

- Understanding How COVID-19 Vaccines Work
- Ensuring COVID-19 Vaccines Work
- Frequently Asked Questions about COVID-19 Vaccination
- Examples of Workers Who May Get Pfizer-BioNTech Booster Shots
- COVID-19 Vaccines for Moderately to Severely Immunocompromised People

For Healthcare and Public Health

Considerations for Use of a COVID-19 Vaccine Booster Dose

More Information

ACIP Presentation Slides, October 21, 2021

ACIP Presentation Slides, September 22–23, 2021

Last Updated Oct. 27, 2021

CDC Centers for Disease Control and Prevention

COVID-19

COVID-19 Vaccine Equity for Racial and Ethnic Minority Groups

Updated Nov. 2, 2021

CDC is committed to COVID-19 vaccine equity, which is when everyone has fair and just access to COVID-19 vaccination. There are many social, geographic, political, economic, and environmental factors that create challenges to vaccination access and acceptance, and that often affect racial and ethnic minority groups. Some of these factors include:

- Education, income, and wealth gaps
- Job access and working conditions
- Racism and other forms of discrimination
- Gaps in healthcare access
- Transportation and neighborhood conditions
- Lack of trust as a result of past medical racism and experimentation

Because of these and other challenges, some Black or African American people and Hispanic or Latino people are less likely to be vaccinated against COVID-19 than people in other racial and ethnic minority groups and non-Hispanic White people.[1-3] You can view the most current race and ethnicity data on COVID-19 vaccination. In addition to being less likely to get a vaccine, Black or African American people and Hispanic or Latino people are more likely to get seriously ill and die from COVID-19 due to the factors listed above.[4-6] CDC uses the Social Vulnerability Index (SVI) to assess the potential negative effects on communities caused by external stresses on human health. You can view the most current health equity data on COVID-19.

Other racial and ethnic minority groups, including American Indian or Alaska Native people, have also been more severely affected by COVID-19 than non-Hispanic White people, due to the challenges listed above. However, vaccination rates among American Indian or Alaska Native people are the highest among racial and ethnic minority groups, [7] in part due to vaccination efforts from CDC and partners. You can find more information about CDC COVID-19 activities in Tribal communities, including vaccination efforts, and communication resources.

CDC Is Committed to Vaccine Equity for Racial and Ethnic

Minority Groups

CDC is paving the way in vaccine equity efforts with national, state, tribal, territorial, local, and community partners to ensure that Black or African American people and Hispanic or Latino people have fair and just access to COVID-19 vaccination. To support vaccine equity, CDC continues to communicate with and listen to all communities affected by COVID-19. CDC is working to build trust, increase collaboration, and create tools and resources to respond to the concerns and feedback from all communities affected by COVID-19, especially those disproportionately impacted. These activities, along with messages supported by science, can help to increase COVID-19 vaccine acceptance and make it easier to get vaccinated.

Communication and Educational Resources

You can use the resources below to engage with communities that have been affected by COVID-19. Many of the resources available can be tailored for racial and ethnic minority communities to:

- Help build vaccine confidence
- Share clear and accurate information to educate about COVID-19
- Raise awareness about the benefits of vaccination and address common questions and concerns
- Adapt key messages to the language, tone, and format that will resonate with communities
- Understand community needs regarding COVID-19 vaccines

COVID-19 Vaccines for Children and Teens: Resources for parents and caregivers to help find COVID-19 vaccines for children and information about COVID-19 vaccination for children 5 years and older.

COVID-19 Vaccination for Children 5-11 Years Old: Information for providers, jurisdictions, and partners planning vaccination of children, clinical research, and information for children with developmental disabilities.

A Guide for Community Partners—Increasing COVID-19 Vaccine Uptake Among Racial and Ethnic Minority Communities : A resource for community organizations to engage in or support COVID-19 vaccination confidence and access in racial and ethnic minority communities. Explore strategies, interventions, and ready-made messages and materials. This document is also available in Spanish .

COVID-19 Vaccination Toolkit for Health Departments and Other Public Health Partners and Community-Based Organizations Vaccine Toolkit: Include key messages and community engagement strategies that build trust and educate communities about COVID-19 vaccines.

Communication Toolkit for Migrants, Refugees, and Other Limited- English-Proficient Populations: Prevention and vaccination messaging for public health professionals, health care providers, and community organizations to reach communities that speak languages other than English.

Rapid Community Assessment Guide: Resources for state and local health departments to identify communities at risk for low COVID-19 vaccine uptake and understand community needs regarding COVID-19 vaccination.

COVID-19 Vaccination for Essential Workers: Racial and ethnic minority groups are disproportionately represented among essential work and industries. This page includes resources for employees and employers to help plan for and encourage COVID-19 vaccination to protect the workplace.

CDC has printable resources covering a wide range of topics related to COVID-19 vaccines that can be filtered by audience.

- Facts About COVID-19 Vaccines: General information about COVID-19 vaccines. Available in 27 languages.
- What to Expect after Getting a COVID-19 Vaccine: Information on what to expect after getting a COVID-19 vaccine. Available in 10 languages.
- COVID-19 Vaccine for Preteens and Teens: Resource for parents on COVID-19 vaccines for preteens and teens. Information on COVID-19 vaccine for children and teens is also available in Spanish.
- A Safe and Effective COVID-19 Vaccine is Now Available: Comic-book style graphic fotonovela that tells the story of a daycare worker's decision to get vaccinated against COVID-19. Available in English, Spanish, and Haitian Creole.

CDC Partnerships and Funding

Health and vaccine equity are essential parts of CDC's mission. CDC works with national, state, tribal, territorial, local, and community partners to promote COVID-19 vaccination among Black or African American people and Hispanic or Latino people. To support these partnerships, CDC has provided funding for organizations that reach racial and ethnic minority groups. This funding includes:

- $3 billion awarded to 64 jurisdictions to support local health departments and community-based organizations in launching new programs and initiatives to increase vaccine access, acceptance, and uptake in communities disproportionately impacted by COVID-19
- $2.25 billion awarded to health departments across the United States and its territories to work in collaboration with community partners to support efforts to address COVID-19 health disparities
- $348 million to organizations for community health worker (CHW) services to support COVID-19 prevention and control, and $32 million to organizations for CHW services to support training, technical assistance, and evaluation, all funded through the CDC's Community Health Workers for COVID Response and Resilient Communities initiative.

Additional CDC efforts toward vaccine equity for racial and ethnic minority groups include funding for:

- 8 national organizations through CDC's Partnering with National Organizations to Increase Vaccination Coverage Across Different Racial and Ethnic Adult Populations Currently Experiencing Disparities , including: Asian and Pacific Islander American Health Forum, National Alliance for Hispanic Health, National Minority Quality Forum, National Urban League, Northwest Portland Area Indian Health Board, National Council of Negro Women, UnidosUS, Conference of National Black Churches
- 4 medical organizations serving racial and ethnic minority groups through CDC's Partnering with Professional and Medical Associations to Increase Vaccination Coverage Across Different Racial and Ethnic Adult Populations Experiencing Disparities , including: National Medical Association, National Hispanic Medical Association, Association of American Indian Physicians, National Council of Urban Indian Health
- 3 national foundations through CDC's Partnering with National Organizations to Support Community-Based Organizations to Increase Vaccination Coverage Across Different Racial and Ethnic Adult Populations Currently Experiencing Disparities , including: CDC Foundation, Community Catalyst, Urban Institute
- 34 national, state, tribal, and community organizations through CDC's Racial and Ethnic Approaches to Community Health – REACH , including: Alaska Native Tribal Health Consortium, Allegheny County, PA, American Heart Association, California Department of Public Health, Cicatelli Associates, Inc., City of Hartford, CT, City of Miami Gardens, FL, City of San Antonio Metropolitan Health District, TX, City of Worcester, MA, County of San Diego, Health and Human Services Agency, CA, Cuyahoga County Board of Health, Dekalb County Board of Health, GA, Eastern Michigan University, Health and Hospital Corporation of Marion County, Health Partners Initiative DBA Partnership for a Healthy Lincoln, NE, Houston County Board of Health, TX, Leadership Council for Healthy Communities, Lowell Community Health Center, Mississippi Public Health Institute, Montgomery Area Community Wellness Coalition, AL, Multnomah County Health Department, National Kidney Foundation of Michigan, Partners in Health, Penn State Health Milton S. Hershey Medical Center, Pima County Health Department, AZ, Presbyterian Healthcare Services, Public Health Advocates, Rosedale Assistance & Opportunities, Seattle-King County Public Health Department, WA, Southern Nevada Health District, The Institute for Family Health, University of Arkansas for Medical Sciences, YMCA of Coastal Georgia

Through these and other partnerships, CDC is working to remove barriers to COVID-19 vaccination access and promote vaccine equity. In line with this effort, CDC works with the Federal Retail Pharmacy Program to conduct community-based activities and use data to ensure COVID-19 vaccines are accessible in all communities.

Because of the availability of COVID-19 vaccines, the nation is closer than ever to ending the COVID-19 pandemic in the United States. Yet challenges remain in ensuring all people have fair and just access to COVID-19 vaccination. CDC is committed to ongoing work to promote vaccine equity.

Resources on COVID-19 and Health Equity

CDC Health Equity Resources

- COVID Data Tracker's Health Equity Landing Page

- COVID-19 Racial and Ethnic Health Disparities
- Health Equity in Action
- Health Equity: Promoting Fair Access to Health

Other Resources

- Emory University's COVID-19 Health Equity Interactive Dashboard
- Morehouse School of Medicine, Satcher Health Leadership Institute's Health Equity Tracker
- National Academy of Medicine's Resources on Health Equity in the Context of COVID-19 & Disproportionate Outcomes for Marginalized Groups

Footnotes

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7. CDC COVID Data Tracker Vaccination Demographics Trends

Last Updated Nov. 2, 2021

COVID-19 Vaccines

The FDA has regulatory processes in place to facilitate the development of COVID-19 vaccines that meet the FDA's rigorous scientific standards.

Español (/about-fda/fda-en-espanol/informacion-sobre-las-vacunas-para-el-covid-19)

October 29, 2021: **The FDA expands emergency use authorization of the Pfizer-BioNTech COVID-19 Vaccine to include children 5 through 11 years of age.** Read the press release (/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age) and watch the press conference (https://youtu.be/WLbGnS-kqTY) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).

October 20, 2021: **The FDA expands authorizations for COVID-19 vaccine booster doses for eligible populations who received the Pfizer-BioNTech or Moderna COVID-19 Vaccine** and **for Janssen COVID-19 Vaccine recipients 18 and older.** Read the press release and listen to the media call (https://youtu.be/rou7tf4vaUU) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).

On this page:

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COVID-19 Vaccines Authorized for Emergency Use or FDA-Approved

Comirnaty and Pfizer-BioNTech COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine)

Moderna COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine)

Janssen COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine)

Fact sheets for health care providers and patients included
Report vaccine side effects toll-free at 1-800-822-7967 or online (https://vaers.hhs.gov/reportevent.html)

FDA COVID-19 Vaccine News and Updates

Type of Information

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Date	Update	Type
10/29/2021	**Coronavirus (COVID-19) Update** (/news-events/press-announcements/coronavirus-covid-19-update-october-29-2021) The FDA discussed the agency's actions to expand the use of a single booster dose for COVID-19 vaccines in eligible populations. In addition, the FDA authorized the 11th over-the-counter (OTC) COVID-19 test and is investigating certain imported medical gloves that appear to have been reprocessed, cleaned or recycled and sold as new.	COVID-19 Update
10/29/2021	**FDA Authorizes COVID-19 Vaccine in Children 5 through 11** (/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age) The authorization was based on the FDA's thorough and transparent evaluation of the data that included input from independent advisory committee experts who overwhelmingly voted in favor of making the vaccine available to children in this age group.	Press Release / Public Statement
10/26/2021	**Vaccines and Related Biological Products Advisory Committee Meeting** (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-october-26-2021-meeting-announcement) The committee will discuss a request to amend Pfizer-BioNTech's Emergency Use Authorization (EUA) for administration of their COVID-19 mRNA vaccine to children 5 through 11 years of age. View livestream (https://youtu.be/laaL0_xKmmA) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).	Event

Showing 1 to 3 of 131 entries

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FDA Leaders on Vaccines

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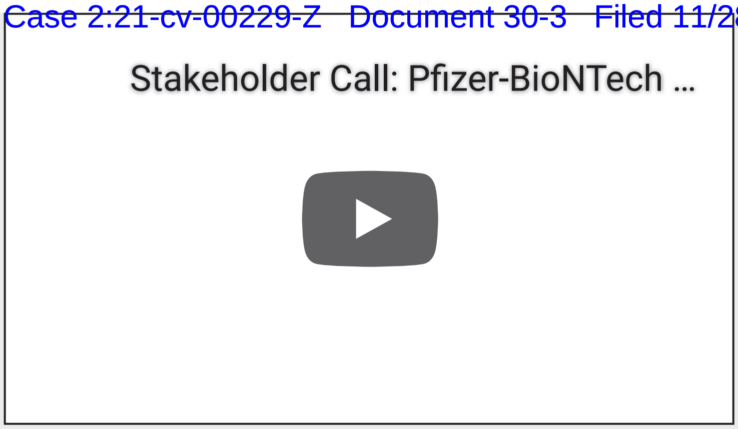

Acting FDA Commissioner, Janet Woodcock, M.D. and Director, FDA Center for Biologics Evaluation and Research, Peter Marks, M.D., Ph.D., discuss the Pfizer-BioNTech COVID-19 Vaccine booster dose. (44:22)

Preparing for the School Year: Younger Children & Adolescent Vaccine Updates (https://youtu.be/F2wNTDZh9zY) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

FDA's Dr. Peter Marks speaks during a webinar on COVID-19 vaccines for children and adolescents. *(August 13, 2021)*

Myocarditis and Pericarditis Updates (https://youtu.be/_j8ziaOpl7o) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

Acting FDA Commissioner Janet Woodcock, M.D. and the Director of FDA's Center for Biologics Evaluation and Research, Peter Marks, M.D., Ph.D., discuss the suggested increased risks of myocarditis and pericarditis following COVID19 vaccination. *(June 29, 2021)*

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Making It Plain Town Hall (https://youtu.be/IKZcODs56O8) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

Director of FDA's Center for Biologics Evaluation and Research Dr. Peter Marks discusses COVID-19 vaccines during a Town Hall with leaders of The Black Coalition Against COVID-19 *(June 29, 2021)*

Emergency Use Authorization — Vaccines (https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#vaccines)

Emergency Use Authorization for Vaccines Explained (/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained)

Questions and answers on vaccine EUAs

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The Path for a COVID-19 Vaccine from Research to Emergency Use Authorization (PDF, 723KB) (/media/143890/download)

A 1-page PDF infographic, also in: Español - Spanish (PDF-616KB) (/media/144116/download)

简体中文 - Chinese (PDF-200KB) (/media/144350/download)

Tagalog (PDF-185KB) (/media/144346/download)

한국어 - Korean (PDF-242KB) (/media/144351/download)

Việt - Vietnamese (PDF-177KB) (/media/144348/download)

ᏣᎳᎩ - Cherokee (PDF-249KB) (/media/144381/download)

Diné Bizaad - Navajo (PDF-257KB) (/media/144382/download)

Video Frequently Asked Questions

Q: What are the ingredients in the COVID vaccines?

Ask an Expert: What are the ingred...

Q: Do the COVID vaccines cause long-term health problems?

Ask an Expert: Do the COVID vacci...

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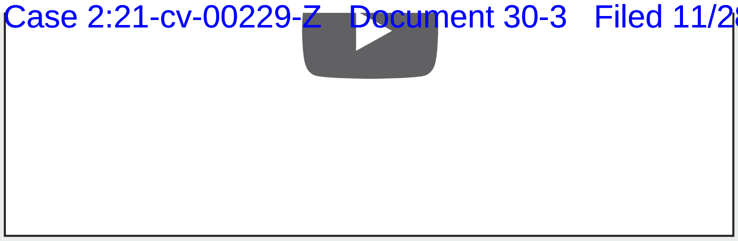
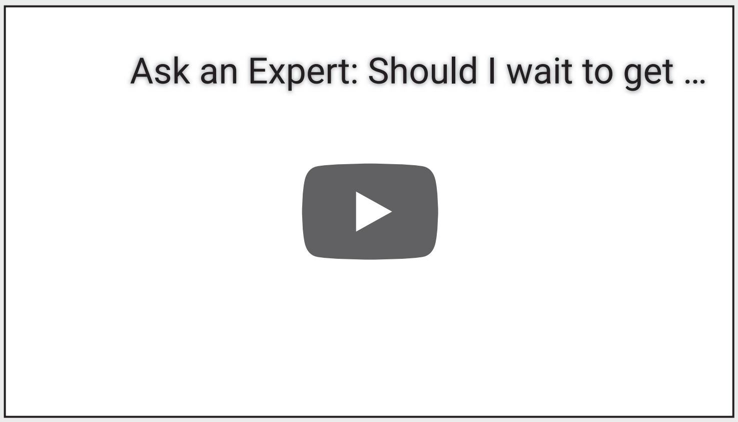
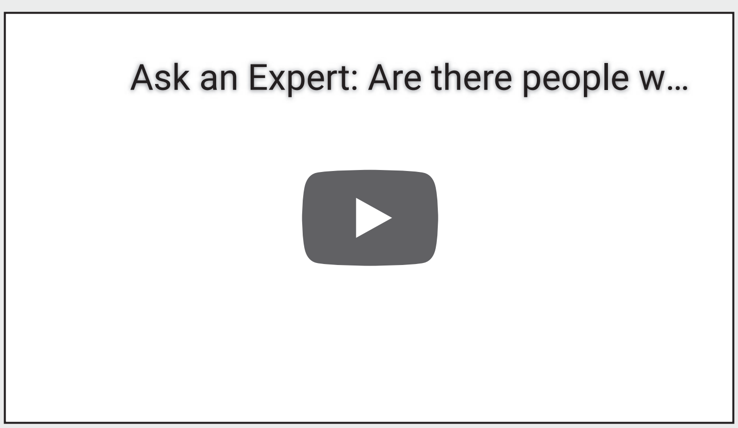


Q: Should I wait to get a COVID vaccine?



Q: Are there people who are eligible but shouldn't get a COVID-19 vaccine?



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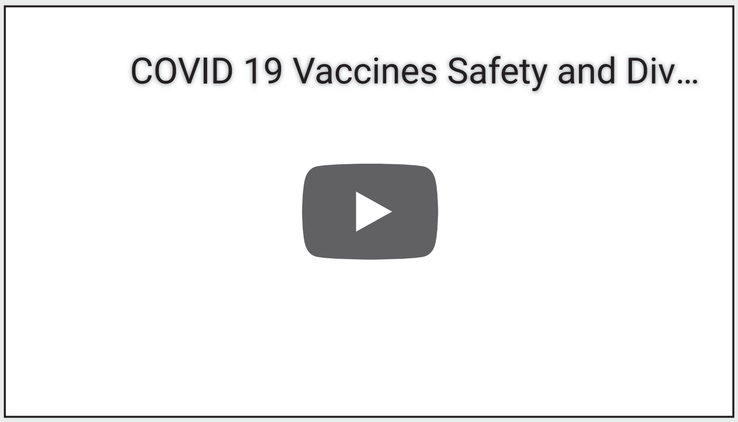
Vaccine Basics



Diverse researchers and scientists who mirror the diversity in our communities have been developing vaccines to help protect us from COVID-19. Learn why you and your loved ones should get vaccinated as soon as a vaccine is available to you. (1:22)

Español (https://youtu.be/2Yk74obIje0) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) 한국의 (https://youtu.be/7vg-yzexSWU) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) Navajo (https://youtu.be/ogKcp7S-moE) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

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Vaccine Development 101 (/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101)

Typical vaccine development process starting in the lab through post-FDA-approval monitoring

The Path for Vaccines from Research to FDA Approval (/media/151716/download)

Infographic on the path for vaccines from research to FDA approval

Español (https://www.fda.gov/media/152219/download)

COVID-19 Vaccine Safety Surveillance (/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance)

Ongoing FDA monitoring of COVID-19 vaccine safety

Learn More About COVID-19 Vaccines From the FDA (/consumers/consumer-updates/learn-more-about-covid-19-vaccines-fda)

Answers to common questions about COVID-19 vaccines

Vaccine Podcasts

Podcast: COVID-19 Vaccine Boosters and COVID-19 Vaccines for Kids (https://omny.fm/shows/in-the-bubble/the-fda-commissioner-on-boosters-vaccines-for-kids) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

Acting FDA Commissioner Dr. Janet Woodcock discusses additional shots of the COVID-19 vaccine ("boosters") and COVID-19 vaccines for kids under 12

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Health Equity Podcast: The Emergency Use Authorization (EUA) Process (/consumers/health-equity-forum-podcast/conversation-fda-chief-scientist-learn-about-emergency-use-authorization-eua-process)

RADM Araojo discusses FDA's Emergency Use Authorization process with RADM Denise Hinton, FDA's Chief Scientist

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Radio Interview: How FDA Collaborated on COVID-19 Vaccines (https://federalnewsnetwork.com/people/2021/06/fda-doctor-recognized-for-collaboration-to-get-covid-vaccines-distributed-at-record-speed/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

Director of the FDA's Center for Biologics Evaluation and Research discusses how the FDA facilitated COVID-19 vaccine development

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Health Equity Podcast: Health Fraud & COVID-19 (/consumers/health-equity-forum-podcast/health-fraud-covid-19-what-you-need-know)

How the FDA works to stop fraudulent products from reaching the market

Publications

USA Today: Interview: Dr. Peter Marks on COVID-19 vaccines for kids under 12 and why the process takes time. (https://www.usatoday.com/story/news/health/2021/09/10/fdas-dr-peter-marks-explains-authorizing-covid-vaccines-children/8276288002/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (9/10/2021)

The Washington Post: Interview: Dr. Peter Marks discusses the process for full approval, also known as licensing, of COVID-19 vaccines. (https://www.washingtonpost.com/health/2021/08/02/coronavirus-vaccines-fda-full-approval-timeline) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (8/2/2021)

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New York Times: Letter to the Editor: The review of applications for full approval of Covid-19 vaccines is one of the highest priorities at the Food and Drug Administration. (https://www.nytimes.com/2021/07/09/opinion/letters/fda-covid-vaccines.html) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (*Subscription may be needed for access*) (7/9/2021)

USA Today: I'm a disabled woman of color. Here's how I overcame my fear of receiving a COVID vaccine. (https://www.usatoday.com/story/opinion/2021/01/14/how-overcame-my-concerns-receiving-covid-19-vaccination-column/6653137002/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (1/14/2021)

USA Today: I'm the FDA point person on COVID-19 vaccines. We'll make sure they're safe and effective. (https://www.usatoday.com/story/opinion/2020/10/27/fda-covid-vaccine-ensuring-safety-and-efficacy-column/6047702002/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (10/27/2020)

Vaccine Advisory Committee Meetings

October 26, 2021 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-october-26-2021-meeting-announcement)

Discussing Data for Pfizer COVID-19 Vaccine for Children 5-11

October 14 - 15, 2021 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-october-14-15-2021-meeting-announcement)

Discussing Moderna COVID-19 Vaccine and Janssen COVID-19 Vaccine Booster Doses

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September 17, 2021 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-september-17-2021-meeting-announcement)

Discussing a Third Dose or "Booster" of a COVID-19 Vaccine

June 10, 2021 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-june-10-2021-meeting-announcement)

Discussing Pediatric Use of COVID-19 Vaccines

February 26, 2021 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-february-26-2021-meeting-announcement)

Discussing Third Emergency Use Authorization Request for a COVID-19 Vaccine

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December 17, 2020 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-17-2020-meeting-announcement)

Discussing Second Emergency Use Authorization Request for a COVID-19 Vaccine

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December 10, 2020 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-10-2020-meeting-announcement)

Discussing First Emergency Use Authorization Request for a COVID-19 Vaccine

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October 22, 2020 (/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-october-22-2020-meeting-announcement)

Discussing, in general, the development, authorization and/or licensure of vaccines to prevent COVID-19

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Vaccine Guidance for Industry

FDA's Center for Biologics Evaluation and Research (CBER) (/vaccines-blood-biologics/industry-biologics/coronavirus-covid-19-cber-regulated-biologics) regulates vaccines and other biological products.

Development and Licensure of Vaccines to Prevent COVID-19 (/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19)

Emergency Use Authorization for Vaccines to Prevent COVID-19 (/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-vaccines-prevent-covid-19)

Vaccine EUA Questions and Answers for Stakeholders (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/vaccine-eua-questions-and-answers-stakeholders)

Required Reporting of Vaccine Side Effects (https://vaers.hhs.gov/reportevent.html)

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Centers for Disease Control and Prevention

COVID-19

Immunocompromised People

Updated Oct. 8, 2021 Print

What You Need to Know

- People with moderately to severely compromised immune systems are especially vulnerable to COVID-19, and may not build the same level of immunity to 2-dose vaccine series compared to people who are not immunocompromised.
- CDC recommends that people with moderately to severely compromised immune systems receive an additional dose of mRNA COVID-19 vaccine at least 28 days after a second dose of Pfizer-BioNTech COVID-19 vaccineor Moderna COVID-19 Vaccine.
- This additional dose is intended to improve immunocompromised people's response to their initial vaccine series

Data on Decreased Immune Response Among Immunocompromised People

People who are moderately to severely immunocompromised make up about 3% of the adult population and are especially vulnerable to COVID-19 because they are more at risk of serious, prolonged illness.

Studies have found that some immunocompromised people don't always build the same level of immunity after vaccination the way non-immunocompromised people do and may benefit from an additional dose to ensure adequate protection against COVID-19. Smaller studies found fully vaccinated immunocompromised people made up a large proportion of hospitalized "breakthrough cases," suggesting immunocompromised people are more likely to transmit the virus to household contacts.

Who Needs an Additional Dose of COVID-19 Vaccine?

Currently, CDC is recommending that moderately to severely immunocompromised people receive an additional dose. This includes people who have

- Been receiving active cancer treatment for tumors or cancers of the blood
- Received an organ transplant and are taking medicine to suppress the immune system
- Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
- Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids or other drugs that may suppress your immune response

People should talk to their healthcare provider about their medical condition, and whether getting an additional dose is appropriate for them.

Find a COVID-19 Vaccine

Find a COVID-19 Vaccine: Search vaccines.gov, text your ZIP code to 438829, or call 1-800-232-0233 to find locations near you.

- Check your local pharmacy's website to see if vaccination walk-ins or appointments are available.
- Contact your state or local health department for more information

Vaccination Card and an Additional Dose

At your first vaccination appointment, you should have received a vaccination card that tells you which COVID-19 vaccine you received, the date you received it, and where you received it. Bring this vaccination card to your additional dose vaccination appointment.

Frequently Asked Questions

How long after getting my initial COVID-19 vaccines can I get an additional dose?

CDC recommends the additional dose of an mRNA COVID-19 vaccine be administered at least 28 days after a second dose of Pfizer-BioNTech COVID-19 vaccine or Moderna COVID-19 vaccine.

Can you mix and match the vaccines?

For people who received either Pfizer-BioNTech or Moderna's COVID-19 vaccine series, a third dose of the same mRNA vaccine should be used. A person should not receive more than three mRNA vaccine doses. If the mRNA vaccine product given for the first two doses is not available or is unknown, either mRNA COVID-19 vaccine product may be administered.

What should immunocompromised people who received Johnson & Johnson's Janssen (J&J/Janssen) vaccine do?

The FDA's recent emergency use authorization amendment only applies to mRNA COVID-19 vaccines, as does CDC's recommendation.

Emerging data have demonstrated that immunocompromised people who have low or no protection following two doses of mRNA COVID-19 vaccines may have an improved response after an additional dose of the same vaccine. There is not enough data at this time to determine whether immunocompromised people who received J&J/Janssen COVID-19 vaccine also have an improved antibody response following an additional dose of the same vaccine.

What are the benefits of people receiving an additional vaccine dose?

An additional dose may prevent serious and possibly life-threatening COVID-19 in people who may not have responded to their initial vaccine series. In ongoing clinical trials, the mRNA COVID-19 vaccines (Pfizer-BioNTech or Moderna) have been shown to prevent COVID-19 following the two-dose series. Limited information suggests that immunocompromised people who have low or no protection after two doses of mRNA vaccines may have an improved response after an additional dose of the same vaccine.

What are the risks of vaccinating individuals with an additional dose?

There is limited information about the risks of receiving an additional dose of vaccine, and the safety, efficacy, and benefit of additional doses of COVID-19 vaccine in immunocompromised people continues to be evaluated. So far, reactions reported after the third mRNA dose were similar to that of the two-dose series: fatigue and pain at injection site were the most commonly reported side effects, and overall, most symptoms were mild to moderate.

As with the two-dose series, serious side effects are rare, but may occur.

What is the difference between an additional dose and a booster shot?

An additional dose is administered to people with moderately to severely compromised immune systems. This additional dose of an mRNA COVID-19 vaccine is intended to improve immunocompromised people's response to their initial vaccine series. A booster shot is administered when a person has completed their vaccine series, and protection against the virus has decreased over time.

If I am immunocompromised do I need an additional dose and a booster shot?

At this time, CDC does not have a recommendation for immunocompromised people to receive both a booster shot and an additional dose. The current recommendation is for immunocompromised people to receive an additional dose 28-days after completing an mRNA COVID-19 vaccine series.

For Healthcare and Public Health

- Talking with Patients Who Are Immunocompromised
- Use of COVID-19 Vaccines Currently Authorized in the United States

Last Updated Oct. 8, 2021

Centers for Disease Control and Prevention

COVID-19

COVID-19 Vaccines for People with Allergies

Updated Mar. 25, 2021 Print

If you get a COVID-19 vaccine and you think you might be having a severe allergic reaction after leaving the vaccination provider site, seek immediate medical care by calling 911. Learn more about COVID-19 Vaccines and Allergic Reactions.

An allergic reaction is considered severe when a person needs to be treated with epinephrine or EpiPen© or if the person must go to the hospital. Experts refer to severe allergic reactions as anaphylaxis.

An **immediate allergic reaction** happens within 4 hours after getting vaccinated and could include symptoms such as hives, swelling, and wheezing (respiratory distress).

If You Are Allergic to an Ingredient in a COVID-19 Vaccine

If you have had a severe allergic reaction or an immediate allergic reaction—even if it was not severe—to any ingredient in an mRNA COVID-19 vaccine, **you should not get either of the currently available mRNA COVID-19 vaccines** (Pfizer-BioNTech and Moderna).

If you have had a severe allergic reaction or an immediate allergic reaction to any ingredient in Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccine, **you should not get the J&J/Janssen vaccine**.

If you aren't able to get one type of COVID-19 vaccine because you are allergic to an ingredient in that vaccine, **ask your doctor if you should get a different type of COVID-19 vaccine**. Learn about the different types of COVID-19 vaccines.

If you had an allergic reaction to a previous shot of an mRNA vaccine

If you aren't able to get the second shot of an mRNA vaccine because you had an allergic reaction to the first shot, **ask your doctor if you should get a different type of COVID-19 vaccine**. Learn about the different types of COVID-19 vaccines.

Information about Specific Vaccines

- Pfizer-BioNTech
- Moderna
- J&J/Janssen

If You Are Allergic to Polyethylene Glycol (PEG) or Polysorbate

PEG and polysorbate are closely related to each other. PEG is an ingredient in the mRNA vaccines, and polysorbate is an ingredient in the J&J/Janssen vaccine.

If you are allergic to PEG, you should not get an mRNA COVID-19 vaccine. Ask your doctor if you can get the J&J/Janssen vaccine.

If you are allergic to polysorbate, you should not get the J&J/Janssen COVID-19 vaccine. Ask your doctor if you can get an mRNA COVID-19 vaccine.

If You Are Allergic to Other Types of Vaccines

If you have had an immediate allergic reaction—even if it was not severe—to a vaccine or injectable therapy for another disease, **ask your doctor if you should get a COVID-19 vaccine.** Your doctor will help you decide if it is safe for you to get vaccinated.

If You Have Allergies Not Related to Vaccines

CDC recommends that people get vaccinated even if they have a history of severe allergic reactions not related to vaccines or injectable medications—such as food, pet, venom, environmental, or latex allergies. People with a history of allergies to oral medications or a family history of severe allergic reactions may also get vaccinated.

Find a COVID-19 Vaccine: Search vaccines.gov, text your ZIP code to 438829, or call 1-800-232-0233 to find locations near you in the U.S.

Related Pages

- What to Do If You Have an Allergic Reaction after Getting a COVID-19 Vaccine
- Different COVID-19 Vaccines

For Healthcare Professionals

- Management of Anaphylaxis after COVID-19 Vaccination
- COVID-19 Clinical Resources

Last Updated Mar. 25, 2021

Centers for Disease Control and Prevention

COVID-19

COVID-19 Vaccines Work

Updated Aug. 16, 2021 Print

What You Need to Know

- Research shows that all COVID-19 vaccines authorized for use in the United States provide protection against COVID-19.
- CDC and other experts are continuing to assess how COVID-19 vaccines work in real-world conditions. These types of studies are called "vaccine effectiveness" studies.

What We Know about How Well COVID-19 Vaccines Are Working

COVID-19 vaccination reduces the risk of COVID-19 and its potentially severe complications. All COVID-19 vaccines currently authorized for use in the United States helped protect people against COVID-19, including severe illness, in clinical trial settings. So far, studies that have looked at how COVID-19 vaccines work in real-world conditions (vaccine effectiveness studies) have shown that these vaccines are working well.

Most vaccine effectiveness data now available are related to mRNA vaccines (Pfizer-BioNTech and Moderna) because these vaccines have been available longer. CDC and other experts continue to study the effectiveness of both mRNA vaccines and the Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccine in real-world conditions.

So Far, Research on mRNA COVID-19 Vaccine Effectiveness in Real-World Conditions Is Reassuring

Vaccine effectiveness studies provide a growing body of evidence that mRNA COVID-19 vaccines offer similar protection in real-world conditions as they have in clinical trial settings, reducing the risk of COVID-19, including severe illness, among people who are fully vaccinated by 90 percent or more. Most vaccine effectiveness data now available are related to mRNA vaccines. Data related to the J&J/Janssen vaccine will be shared when available.

In addition to providing protection against COVID-19, there is increasing evidence that COVID-19 vaccines also provide protection against COVID-19 infections without symptoms (asymptomatic infections). COVID-19 vaccination can reduce the spread of disease overall, helping protect people around you.

Research Suggests That for mRNA COVID-19 Vaccines, Two Doses Are Better than One

Real-world data from vaccine effectiveness studies have shown that receiving only one dose of these mRNA COVID-19 vaccines provides some protection against COVID-19, at least in the short term. These studies have also shown that for mRNA vaccines, two doses provide better protection than one dose. To receive the most benefit from vaccination, people should get the recommended number of doses of vaccine.

COVID-19 Vaccines Help Protect against Severe Illness with COVID-19 Vaccine Breakthrough Cases

While COVID-19 vaccines are working well, some people who are fully vaccinated against COVID-19 will still get sick, because no vaccines are 100% effective. These are called vaccine breakthrough cases. However, data suggest that vaccination may make symptoms less severe in people who are vaccinated but still get COVID-19. mRNA COVID-19 vaccines have been shown to provide protection against severe illness and hospitalization among people of all ages eligible to receive them. This includes people 65 years and older who are at higher risk of severe outcomes from COVID-19.

It typically takes about 2 weeks for the body to build protection after vaccination. You are fully vaccinated two weeks after your second dose of Pfizer -BioNTech or Moderna vaccine and two weeks after your single dose of Johnson & Johnson's J&J/Janssen vaccine. It is possible you could still get COVID-19 soon after vaccination because your body has not had enough time to build protection. Keep taking precautions until you are fully vaccinated.

People who have a condition or are taking medications that weaken their immune system may not be fully protected even if they are fully vaccinated. They should continue to take all precautions recommended for unvaccinated people, including wearing a well-fitted mask, until advised otherwise by their healthcare provider.

CDC Recommends

- Get a COVID-19 vaccine as soon as you can.
- To get the most protection, get all recommended doses of a COVID-19 vaccine.

Variants and Vaccines

- FDA-authorized COVID-19 vaccines help protect against Delta and other known variants.
- These vaccines are effective at keeping people from getting COVID-19, getting very sick, and dying.
- To maximize protection from the Delta variant and prevent possibly spreading it to others, you should wear a mask indoors in public if you are in an area of substantial or high transmission even if you are fully vaccinated.
- We don't know how effective the vaccines will be against new variants that may arise.

More details: Learn more about COVID-19 variants.

Last Updated Aug. 16, 2021

Centers for Disease Control and Prevention

Daily Updates of Totals by Week and State

Provisional Death Counts for Coronavirus Disease 2019 (COVID-19)

Contents

Updated: November 15, 2021

Note: Provisional death counts are based on death certificate data received and coded by the National Center for Health Statistics as of November 15, 2021. Death counts are delayed and may differ from other published sources (see Technical Notes). Counts will be updated periodically. Additional information will be added to this site as available.

The provisional counts for coronavirus disease 2019 (COVID-19) deaths are based on a current flow of mortality data in the National Vital Statistics System. National provisional counts include deaths occurring within the 50 states and the District of Columbia that have been received and coded as of the date specified. It is important to note that it can take several weeks for death records to be submitted to National Center for Health Statistics (NCHS), processed, coded, and tabulated. Therefore, the data shown on this page may be incomplete, and will likely not include all deaths that occurred during a given time period, especially for the more recent time periods. Death counts for earlier weeks are continually revised and may increase or decrease as new and updated death certificate data are received from the states by NCHS. COVID-19 death counts shown here may differ from other published sources, as data currently are lagged by an average of 1–2 weeks.

The provisional data presented on this page include the provisional counts of deaths in the United States due to COVID-19, deaths from all causes and percent of expected deaths (i.e., number of deaths received over number of deaths expected based on data from previous years), pneumonia deaths (excluding pneumonia deaths involving influenza), pneumonia deaths involving COVID-19, influenza deaths, and deaths involving pneumonia, influenza, or COVID-19; by week ending date, month, and year, and specific jurisdictions.

For the Index of Provisional COVID-19 Mortality Surveillance and Ad-hoc Data Files, click here.
Table 1 has counts of deaths involving COVID-19 and other select causes of death by time-period in which the death occurred.
For data on deaths involving COVID-19 by time-period and jurisdiction, Click here to download.

Table 1. Deaths involving coronavirus disease 2019 (COVID-19), pneumonia, and influenza reported to NCHS by me-period and jurisdic on of occurrence.

Data as of:

11/15/2021

State

United States

Week ending date in which the death occurred	All Deaths involving COVID-19 [1]	Deaths from All Causes	Percent of Expected Deaths [2]	Deaths involving Pneumonia [3]	Deaths involving COVID-19 and Pneumonia [3]	All Deaths involving Influenza [4]	Deaths involving Pneumonia, Influenza, or COVID-19 [5]
11/13/2021	612	6,538	12	620	345	0	887
11/6/2021	2,997	28,540	53	2,932	1,727	0	4,202
10/30/2021	5,235	44,221	83	5,053	3,095	5	7,197
10/23/2021	7,303	54,860	103	6,715	4,376	13	9,649
10/16/2021	8,840	59,929	115	7,894	5,331	8	11,409
10/9/2021	10,412	63,483	121	9,063	6,405	18	13,084
10/2/2021	12,031	66,560	128	10,038	7,329	16	14,751
9/25/2021	13,724	68,344	132	11,112	8,342	16	16,507
9/18/2021	14,726	69,942	136	11,805	8,982	16	17,560
9/11/2021	14,927	70,497	138	11,938	9,199	15	17,674
9/4/2021	15,069	70,730	139	12,035	9,366	28	17,755
8/28/2021	13,860	69,819	138	11,267	8,452	16	16,683
8/21/2021	11,951	68,034	134	9,982	7,180	11	14,759
8/14/2021	9,213	65,246	128	8,361	5,583	11	11,998
Total	**761,930**	**6,219,510**		**685,653**	**392,065**	**9,588**	**1,063,742**

Weekly Monthly Yearly

Microsoft Power BI 1 of 3

NOTE: Empty data cells represent death counts between 1-9 that have been suppressed in accordance with NCHS confidentiality standards. Number of deaths reported in this table are the total number of deaths received and coded as of the date of analysis and may not represent all deaths that occurred in that period. Counts of deaths occurring before or after the reporting period are not included in the table. Data during recent periods are incomplete because of the lag in time between when the death occurred and when the death certificate is completed, submitted to NCHS and processed for reporting purposes. This delay can range from 1 week to 8 weeks or more, depending on the jurisdiction and cause of death. The United States population, based on 2020 census estimates from the U.S. Census Bureau, is 331,449,281. United States death counts include the 50 states, plus the District of Columbia and New York City. New York state estimates exclude New York City.

[1] Deaths with confirmed or presumed COVID-19, coded to ICD–10 code U07.1.

[2] Percent of expected deaths is the number of deaths for all causes for these time-periods in 2020 or 2021 compared to the average number across the same time-period in 2017–2019. Previous analyses of 2015–2016 provisional data completeness have found that completeness is lower in the first few weeks following the date of death (<25%), and then increases over time such that data are generally at least 75% complete within 8 weeks of when the death occurred (8).

[3] Counts of deaths involving pneumonia (J12.0-J18.9) include pneumonia deaths that also involve COVID-19 and exclude pneumonia deaths involving influenza.

[4] Counts of deaths involving influenza (J09-J11) include deaths with pneumonia or COVID-19 also listed as a cause of death.

[5] Deaths with confirmed or presumed COVID-19, pneumonia, or influenza, coded to ICD–10 codes U07.1 or J09–J18.9.

Understanding the Numbers: Provisional Death Counts and COVID-19

Provisional death counts deliver the most complete and accurate picture of lives lost to COVID-19. They are based on death certificates, which are the most reliable source of data and contain information not available anywhere else, including comorbid conditions, race and ethnicity, and place of death.

How it Works

The National Center for Health Statistics (NCHS) uses incoming data from death certificates to produce provisional COVID-19 death counts. These include deaths occurring within the 50 states and the District of Columbia.

NCHS also provides summaries that examine deaths in specific categories and in greater geographic detail, such as deaths by county and by race and Hispanic origin.

COVID-19 deaths are identified using a new ICD–10 code. When COVID-19 is reported as a cause of death – or when it is

COVID-19 deaths are identified using a new ICD–10 code. When COVID-19 is reported as a cause of death – or when it is listed as a "probable" or "presumed" cause — the death is coded as **U07.1**. This can include cases with or without laboratory confirmation.

Why These Numbers are Different

Provisional death counts may not match counts from other sources, such as media reports or numbers from county health departments. Counts by NCHS often track 1–2 weeks behind other data.

- **Death certificates take time to be completed.** There are many steps to filling out and submitting a death certificate. Waiting for test results can create additional delays.
- **States report at different rates.** Currently, 63% of all U.S. deaths are reported within 10 days of the date of death, but there is significant variation between states.
- **It takes extra time to code COVID-19 deaths.** While 80% of deaths are electronically processed and coded by NCHS within minutes, most deaths from COVID-19 must be coded by a person, which takes an average of 7 days.
- **Other reporting systems use different definitions or methods for counting deaths.**

Things to know about the data

Provisional counts are not final and are subject to change. Counts from previous weeks are continually revised as more records are received and processed.

Provisional data are not yet complete. Counts will not include all deaths that occurred during a given time period, especially for more recent periods. However, we can estimate how complete our numbers are by looking at the average number of deaths reported in previous years.

Death counts should not be compared across states. Some states report deaths on a daily basis, while other states report deaths weekly or monthly. State vital record reporting may also be affected or delayed by COVID-19 related response activities.

For more detailed technical information, visit the Provisional Death Counts for Coronavirus Disease 2019 (COVID-19) Technical Notes page.

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Declining prevalence of antibody positivity to SARS-CoV-2: a community study of 365,000 adults

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Abstract

Background

The prevalence and persistence of antibodies following a peak SARS-CoV-2 infection provides insights into its spread in the community, the likelihood of reinfection and potential for some level of population immunity.

Methods

Prevalence of antibody positivity in England, UK (REACT2) with three cross-sectional surveys between late June and September 2020. 365104 adults used a self-administered lateral flow immunoassay (LFIA) test for IgG. A laboratory comparison of LFIA results to neutralization activity in panel of sera was performed.

Results

There were 17,576 positive tests over the three rounds. Antibody prevalence, adjusted for test characteristics and weighted to the adult population of England, declined from 6.0% [5.8, 6.1], to 4.8% [4.7, 5.0] and 4.4% [4.3, 4.5], a fall of 26.5% [-29.0, -23.8] over the three months of the study. There was a decline between rounds 1 and 3 in all age groups, with the highest prevalence of a positive result and smallest overall decline in positivity in the youngest age group (18-24 years: -14.9% [-21.6, -8.1]), and lowest prevalence and largest decline in the oldest group (75+ years: -39.0% [-50.8, -27.2]); there was no change in antibody positivity between rounds 1 and 3 in healthcare workers (+3.45% [-5.7, +12.7]).

The decline from rounds 1 to 3 was largest in those who did not report a history of COVID-19, (-64.0% [-75.6, -52.3]), compared to -22.3% ([-27.0, -17.7]) in those with SARS-CoV-2 infection confirmed on PCR.

Discussion

These findings provide evidence of variable waning in antibody positivity over time such that, at the start of the second wave of infection in England, only 4.4% of adults had detectable IgG antibodies using an LFIA. Antibody positivity was greater in those who reported a positive PCR and lower in older people and those with asymptomatic infection. These data suggest the possibility of decreasing population immunity and increasing risk of reinfection as detectable antibodies decline in the population.

Background

National prevalence surveys of SARS-CoV-2 antibodies provide critical insight into the extent that a population has been exposed to infection and may inform understanding of the future course of the epidemic.[1] Studies in Iceland[2] and Spain[3] found quite different levels of population antibody positivity, with evidence of durable antibody response over 4 months from time of infection seen in Iceland. Meanwhile, cohort studies have suggested that antibody levels in individuals may fall substantially with time after infection, influenced by factors such as the severity of initial illness, age and co-morbidities.[4–9]

Changes in population antibody prevalence over time will be a complex interaction between the incidence of new infections and waning of antibody levels in those previously infected. Sequential antibody prevalence surveys can offer insight into the durability of antibody responses, key to understanding how developing immunity may prevent reinfection and limit further spread in the population.

In England, there was a large and widespread outbreak in March and April 2020 leading to high levels of hospitalisation and deaths.[10] A national lockdown with the closure of schools, universities, hospitality, all but essential retail, and advice to work from home and avoid non-essential travel, was introduced in late March with a marked reduction in new infections until late August 2020.[11]

We have used a home-based testing approach to survey the extent of antibody positivity in the population indicative of SARS-CoV-2 infection. The lateral flow immunoassay (LFIA) employed allows a snapshot of antibody prevalence. Our first national survey in England, carried out among 105,000 individuals in late June 2020, found 6% of the adult population had detectable antibodies. Since the LFIA has a threshold for detection of a positive result, a decline in antibody level in individuals who have been infected may at some point result in

negative tests, that is when the antibody levels fall below the threshold. Thus the proportion of positive tests in sequential random population samples can be used as an indicator of antibody waning.

The time-concentrated nature of the first wave of the UK epidemic provides an opportunity for measuring changes in antibody positivity in the population to estimate waning, and to quantify how this varies by sociodemographic and clinical characteristics. We report here prevalence of detectable antibody across three rounds of surveys (REACT-2 study[12-14]) involving representative cross-sections of the population of England.

Methods

We analysed data from three rounds of a serial cross-sectional study of adults in England, UK that were carried out between June and September 2020 (Table 1). The protocol has been published;[12] briefly, these were random, non-overlapping community samples from the adult population 18 years and older, using a self-administered LFIA test at home.[12–15] Invitations were sent to named individuals randomly selected from the NHS patient list which includes anyone registered with a General Practitioner in England and covers almost the entire population. We aimed for a sample size of 100,000 in rounds 1 and 2 and 150,000 in round 3 to obtain prevalence estimates at lower tier local authority level. Sample size calculations are provided in the protocol,[12] and the number of invitations sent out was based on an assumed response rate of 36 to 38% based on previous surveys. Registration was closed after 125,000 people signed up in rounds 1 and 2, and after 195,000 in round 3. Across all three rounds, 37.7% of those invited registered, and 29.9% provided a valid (IgG positive or negative) result (Supplementary appendix table S1). The response rate declined slightly over the three rounds. Those who registered were posted a self-administered point-of-care LFIA test (Fortress Diagnostics, Northern Ireland) with written and video instructions. The sensitivity

of finger-prick blood (self-read) for IgG antibodies was 84.4% (70.5, 93.5) in RT-PCR confirmed cases in healthcare workers, and specificity 98.6% (97.1, 99.4) in pre-pandemic sera.[16] Participants completed a short registration questionnaire (online/telephone) and a further survey upon completion of their self-test. Survey instruments are available on the study website (https://www.imperial.ac.uk/medicine/research-and-impact/groups/react-study/).

The prevalence from each round was calculated as the proportion of individuals reporting a valid test result who had a positive IgG result, adjusted for test performance,[17] and weighted at national level for age, sex, region, ethnicity and deprivation to the adult population of England (Supplementary Appendix section 1.2). Change in prevalence was calculated between each round and from the first to the third round, and reported at national, regional and local geographic area, plus by key sociodemographic and clinical characteristics. Epidemic curves were constructed retrospectively from information from participants with a positive antibody test who had reported the date of onset for a confirmed or possible case of COVID-19.

To establish the sensitivity of the LFIA in relation to titres of neutralising antibodies we performed live virus neutralization tests on 49 sera from health care workers at 21 days or more since confirmed RT-PCR diagnosis of SARS CoV2 infection.[16] Each of the sera was tested in the laboratory with the Fortress LFIA. In addition, the ability of the sera to neutralise wild type SARS-CoV-2 virus was assessed by neutralisation assay on Vero-E6 cells. Heat-inactivated sera were serially diluted in assay diluent consisting of DMEM (Gibco, Thermo Fisher Scientific) with 1% penicillin-streptomycin (Thermo Fisher Scientific), 0.3% BSA fraction V (Thermo Fisher Scientific). Two-fold serial dilutions starting at 1:10 were incubated with 100 TCID50/well of SARS-CoV-2/England/IC19/2020

diluted in assay diluent for 1 hr at room temperature and transferred to 96-well plates pre-seeded with Vero-E6 cells. Serum dilutions were performed in duplicate. Plates were incubated at 37°C, 5% CO_2 for 4 days before staining the monolayers for surviving cells by adding an equal volume of 2X crystal violet stain to wells for 1 hr. Plates were washed, wells were scored for cytopathic effect and a neutralisation titre calculated as the reciprocal of the highest serum dilution at which full virus neutralisation occurred.

Data were analysed using the statistical package R version 4.0.0.[18]

We obtained research ethics approval from the South Central-Berkshire B Research Ethics Committee (IRAS ID: 283787), and Medicines and Healthcare products Regulatory Agency approval for use of the LFIA for research purposes only. A REACT Public Advisory Group provides input into the design and conduct of the research.

Results

Results were available for 99,908, 105,829 and 159,367 people over the three rounds, which took place approximately 12, 18 and 24 weeks after the peak of the epidemic in England in early April. There were 17,576 positive tests in total. National antibody prevalence, adjusted for test characteristics and weighted to the adult population of England, declined from 6.0% [5.8, 6.1], to 4.8% [4.7, 5.00] and 4.4% [4.3, 4.5], a fall of 26.3% [-29.0, -23.8] over the three rounds. (Table 1, Figure 1) The fall was larger between rounds 1 and 2 (19.0% [-21.8, -16.1]) than between 2 and 3 (-9.1% [-12.0, -6.2]).

Over the three rounds of study we found similar patterns of infection to those reported in round 1[1]. Prevalence was highest for ages 18-24 years and lowest in those aged 75 and over. In the latest round, prevalence remained highest in London, at 9.5% (9.0, 9.9) compared with

1.6% (1.3, 1.9) in the South West of England; people of Black (includes Black Caribbean, African and Black British) and Asian (mainly South Asian) ethnicity had higher prevalence (13.8% [12.6-15.1] and 9.7% [9.1-10.4]) respectively, than those of white ethnicity (3.6% [3.5-3.8]). Prevalence was also higher among people working in health and social (residential) care, those living in more deprived areas and larger households (Table 2).

Table 2 and Figure 2 show the change in prevalence by round and overall by key covariates. There was a decline in prevalence between rounds 1 and 3 in all age groups, with the smallest overall decline at ages 18-24 years (-14.9% [-21.6, -8.1]) and largest at ages 75 years and over (-39.0% [-50.8, -27.2]). The decline from rounds 1 to 3 was largest in those who did not report a history of COVID-19, (-64.0% [-75.6, -52.3]), compared to -22.3% ([-27.0, -17.7]) in those with COVID-19 confirmed on PCR. There was no change in prevalence between rounds 1 and 3 in healthcare workers (+3.45% [-5.7, +12.7]).

Figure 3 shows how antibody prevalence changed between rounds at lower tier local area level (see also maps in Supplementary Appendix Figure 1). The slope of the fitted line approximates to the average decrease in prevalence, and the scatter shows the variation, with some areas seeing an increase and others a large decrease between rounds.

The epidemic curves constructed from people who tested positive and reporting symptoms for each of the three rounds closely overlap, illustrating the relatively short, concentrated outbreak across the country with the majority of cases in March and April. (Figure 4) The figure also shows a steep decline in new cases from 6 April, 2 weeks after the national lockdown was introduced on 23 March. There was limited evidence of new cases after early May overall, but some apparent ongoing transmission in health and social care workers into May and June. (Figure 5). We noted a small increase in cases from late August and early September at the start of the second wave.

To check for consistency between rounds we compared the sensitivity cut-off points between the Fortress LFIA batches used in Round 1 and Rounds 2 and 3 using serial dilutions of sera from 10 PCR-confirmed SARS-CoV-2 infected individuals, and found a high level of consistency (Supplementary appendix figure 2). In laboratory-based assays using sera from health care workers who had recovered from SARS CoV2 infection, we found that a positive result on the LFIA used in the REACT 2 antibody prevalence study was associated with a higher titre of neutralising antibody. Sera that scored positive in the LFIA had a median neutralization titre of 40 which was significantly ($P<0.0001$) higher than those that scored negative with a median of zero (Figure 6).

Discussion

We observe a significant decline in the proportion of the population with detectable antibodies over three rounds of national surveillance, using a self-administered lateral flow test, 12, 18 and 24 weeks after the first peak of infections in England. This is consistent with evidence that immunity to seasonal coronaviruses declines over 6 to 12 months after infection and emerging data on SARS-CoV-2 that also detected a decrease over time in antibody levels in individuals followed in longitudinal studies.[4,5,9] We observed clear differences in rates of decline between groups, for example those reporting SARS-CoV-2 infection based on PCR versus those without a history of COVID-19. In some groups with continued exposure risks no change in prevalence was seen (e.g. healthcare workers).

The relevance of antibody waning for the potential for reinfection by SARS CoV-2 is currently not resolved.[19,20] During any antibody response to an acute pathogen, some level of antibody waning in the months following infection is expected as short lived plasma cells die. Low levels of affinity-matured antibody usually continues to be produced by long-lived

plasma cells, and may be sufficient to maintain levels of antibody that confer immunity. Indeed for some pathogens such as measles, influenza and rhinovirus, antibodies can be detected for many years after infection. However the situation for coronaviruses is less clear. Human challenge studies showed a more profound waning of serum and nasal antibody over one year following coronavirus challenge than was seen for volunteers challenged with rhinovirus. At one year, re-infection with the seasonal coronavirus was observed whereas volunteers who retained antibodies following rhinovirus infection displayed sterilizing immunity. [21,22]

Moreover modelling shows that waning immunity can explain the 1-2 year periodicity of reinfections with seasonal coronaviruses.[23] Although reports of reinfection with SARS-CoV2 have been limited to date,[24] this is in part because definitive evidence of reinfection requires sequencing of virus at two time points, which is rarely available in practice. In addition, asymptomatic testing is not yet widespread in many countries and thus mild or asymptomatic reinfections will go undetected. Understanding the ongoing risks of reinfection for the population is key to understanding the future course of the epidemic.

It is widely thought that titres of anti-Spike (S) antibodies which target the receptor binding domain (RBD, associated with cell entry) correlate with protection from reinfection. [25,26]The lateral flow test used for this study detects antibodies against the spike protein (anti-S), but is qualitative rather than quantitative, and the threshold of detection is not stated in manufacturer's instructions. We tested serial dilutions of known positive sera in the LFIA and confirmed that for each of the sera there was a different dilution after which the LFIA no longer yielded a positive band (Supplementary Appendix Figure 2). This demonstrates that, as antibody wanes from a population with a diverse mixture of starting titres, gradually the proportion of positive individual tests will decline. Our data in Figure 6 suggest the threshold

for detection of antibody in sera with the LFIA corresponds to serum endpoint titres that score between 1:10 and 1:40 in a live virus microneutralisation assay. We cannot know at this time how this relates to the level of antibody that confers protection from infection, though studies in non-human primates vaccinated with an array of vaccines that conferred varying levels of immunity, suggest these may be similar levels to those required for protection.[27] The relevant thresholds for protection in humans who are naturally exposed to virus remain to be defined and will continue to be informed by detailed studies of outbreaks.[28] In addition it is currently not clear what contribution T cell immunity and memory responses will play in protective immunity during re-exposure. As such, it is not possible to say with certainty that the loss of antibody positivity in the LFIA would correlate with an increased risk of an individual being reinfected. However, at a population level, the waning we have observed may indicate an overall decline in the level of population immunity.

The declining prevalence of antibodies raises the question as to the extent to which antibody prevalence estimated during round one of our study, approximately 3 months after the peak of the first wave, may have underestimated the total of those infected in the first wave in the UK. We reported a prevalence of 6.0% (95% CI: 5.8-6.1) from round one (20 June to 13 July 2020), implying that at least 3.36 (3.22, 3.51) million adults in England had been infected with SARS-CoV-2 and tested positive for antibodies.[13] Descriptions of the decline following infection are variable, with a general consensus that IgG levels can remain high for 2-3 months before declining,[9,29] but those with smaller initial antibody responses are likely to decline earlier.[9] Decline may initially be rapid, before plateauing, but data on this are only now beginning to emerge. Our previous estimate of antibody prevalence was consistent with that from the smaller ONS survey which reports antibody prevalence declining from 7.4% (95% CI 5.6, 9.6) in May to 5.6% (5.0, 6.2) in September.[30]

Our study has limitations. It included non-overlapping random samples of the population, but it is possible that people who had been exposed to the virus were less likely to take part over time, which may have contributed to apparent population antibody waning. However, we had similar response rates across the three surveys, and for each round, we re-weighted the sample to be representative of the country as a whole. We adjusted for test characteristics (sensitivity, specificity) based on our evaluation in clinic-based tests among healthcare workers with confirmed infection, carried out before the first round,[16] but changes in prevalence are unlikely to be a consequence of batch variation in tests. We compared the laboratory performance of the LFIAs used in rounds 1 and 2 (where we had seen the strongest decline in positive tests) and found no difference between the two rounds. We also did not detect differences in ability of participants to use the LFIA (indeed, failure rates were lower in later rounds compared to earlier ones). The characteristics of the test mean that results are not appropriate for clinical use in individuals and participants are advised not to change their behaviour based on the result. However, as participants are not blind to the results of their LFIA it is possible that this may have introduced bias into their questionnaire response, but this should not have affected our observation of declining prevalence over time.

In summary, our findings provide evidence of variable waning in antibody positivity over time based on detectable IgG antibodies using a lateral flow assay. These data suggest the possibility of decreasing population immunity and increasing risk of reinfection as detectable antibodies decline in the population.

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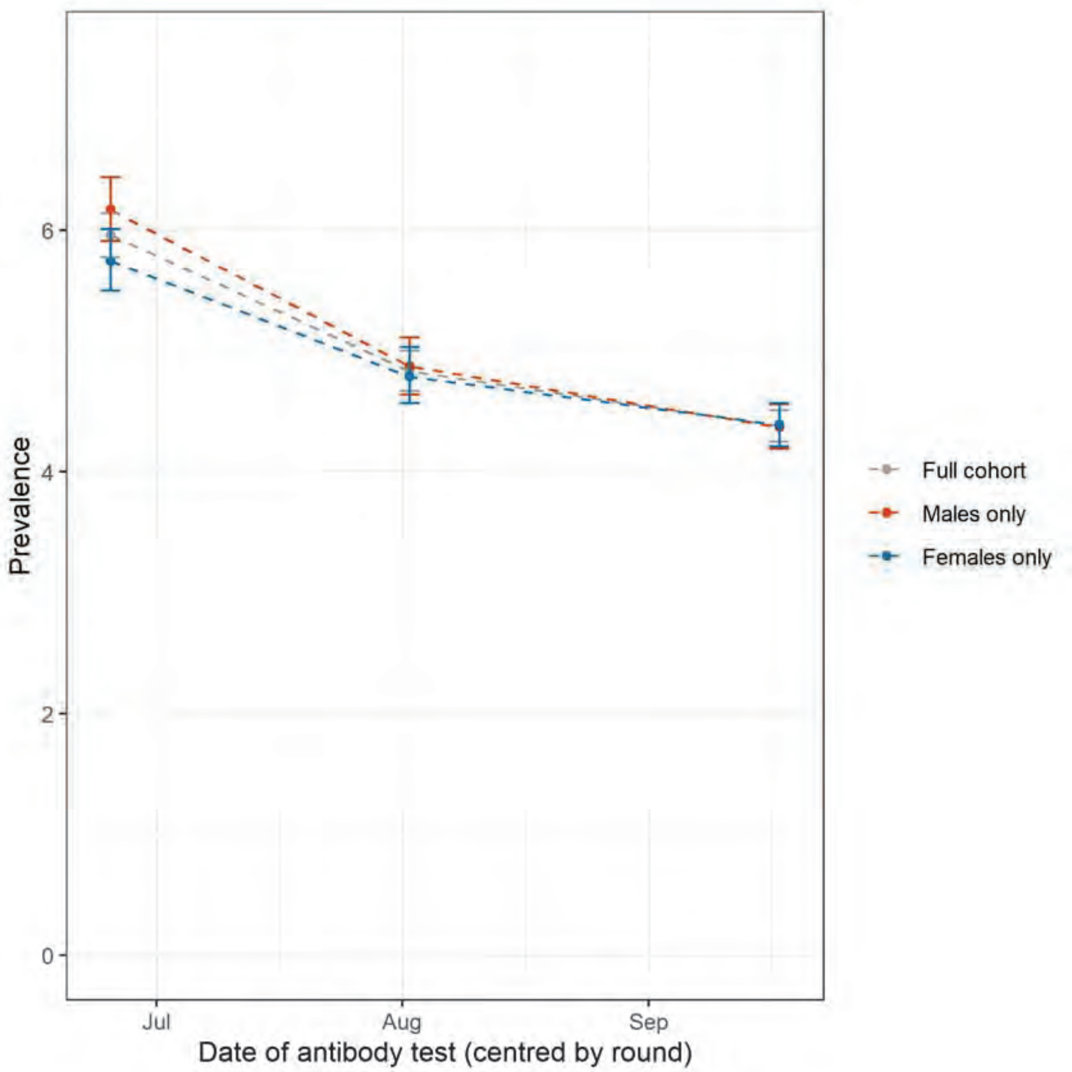
Figures and tables

For Ward, Cooke, Atchison et al. Declining prevalence of antibody positivity to SARS-CoV-2: a community study of 365,000 adults. (26 October 2020)

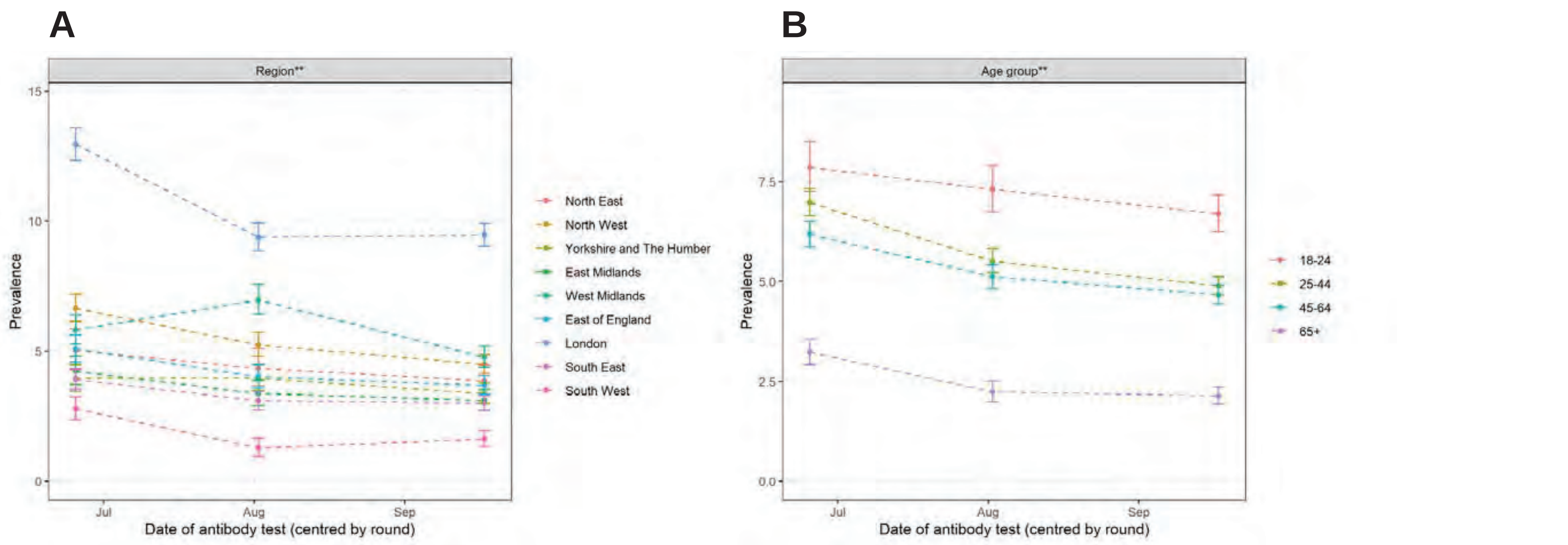
Contents

Figure 1: Prevalence of SARS-CoV-2 IgG antibody in England, by round of study (95% confidence intervals) for full cohort and by sex



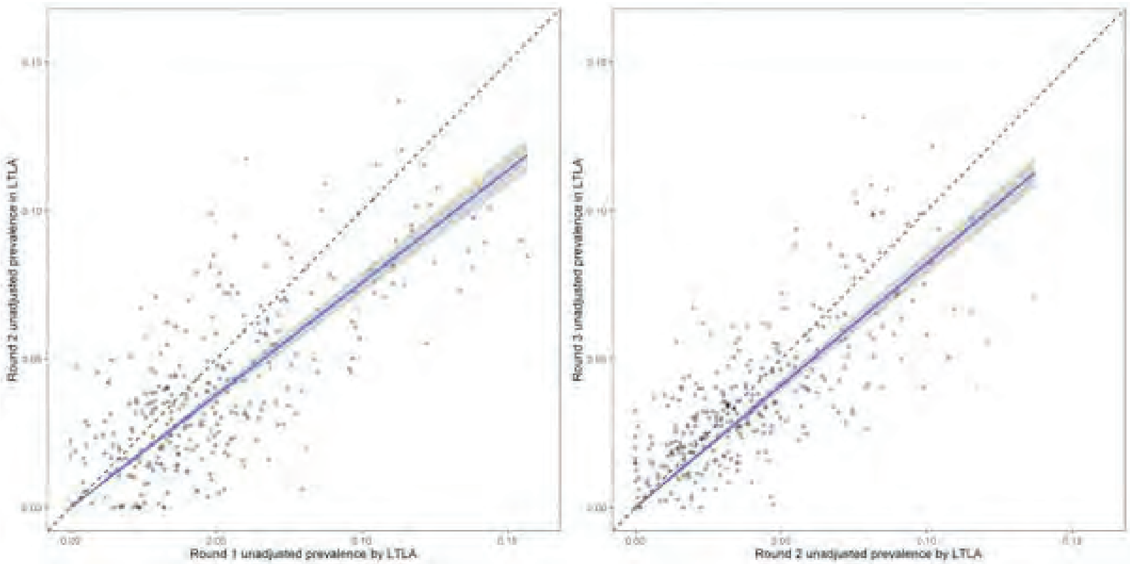
Legend: Dates: Round 1 (June 20 – July 13 2020), Round 2 (31 July – 13 August 2020), Round 3 (15 - 28 September). Points show antibody prevalence by round of study. Prevalences are shown for the full sample (grey line), for male respondents only (red line) and for female respondents only (blue line). Error bars indicate 95% confidence intervals. Data points are aligned with the median response date within each round. All estimates of prevalence (95% confidence intervals) adjusted for imperfect test sensitivity and specificity, and re-weighted to account for sample design and for variation in response rate (age, sex, ethnicity, region and deprivation) to be representative of the England population (18+)

Figure 2 Antibody prevalence for each round of study, by (A) region and (B) age group, June to September 2020



Legend: A) Prevalence in each of the nine regions of England; B) prevalence by age group; Error bars indicate 95% confidence intervals. Prevalences are adjusted for known test performance and re-weighted where appropriate to be representative of the 18+ population of England (** denotes weighted prevalence). Survey responses were received across 2–3 week periods in each round (in late June, early August and mid-September); data points are aligned with the median response date within each round

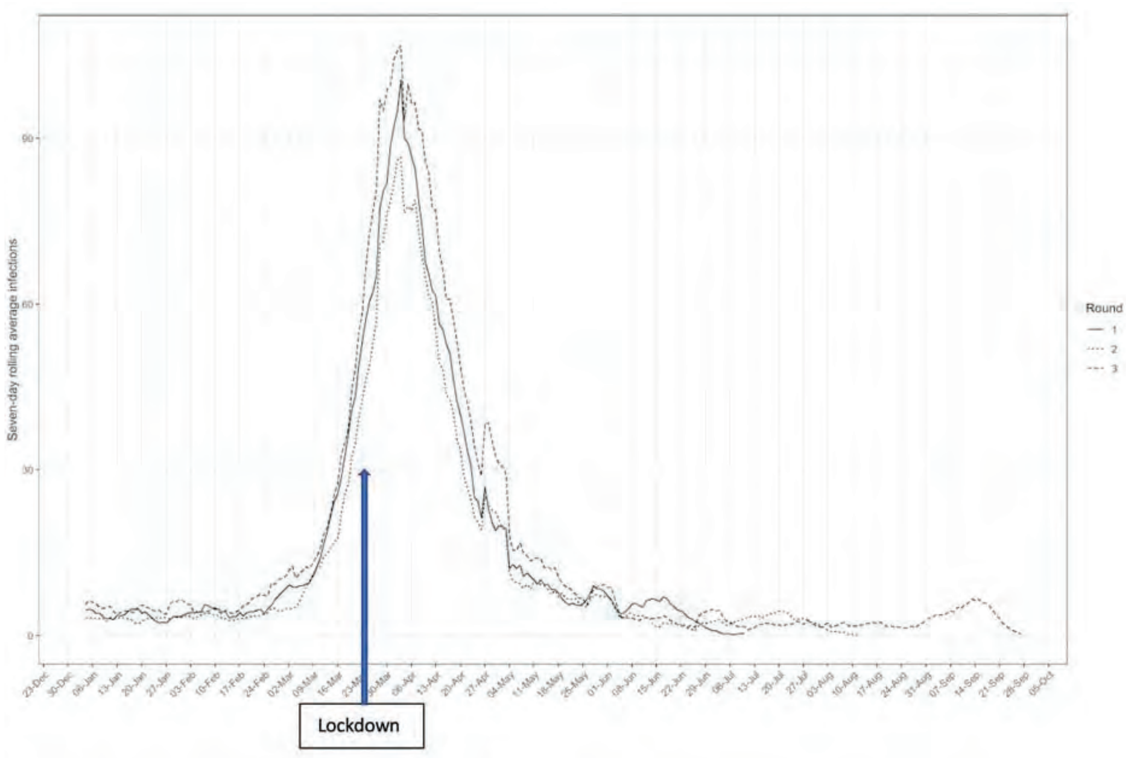
Figure 3 Antibody prevalence between rounds 1 and 2, and 2 and 3 by lower tier local authority



Regression: R2 vs R1 = 0.620, 38% reduction
R3 vs R2 = 0.846, 15% reduction
R3 vs R1 = 0.594, 41% reduction

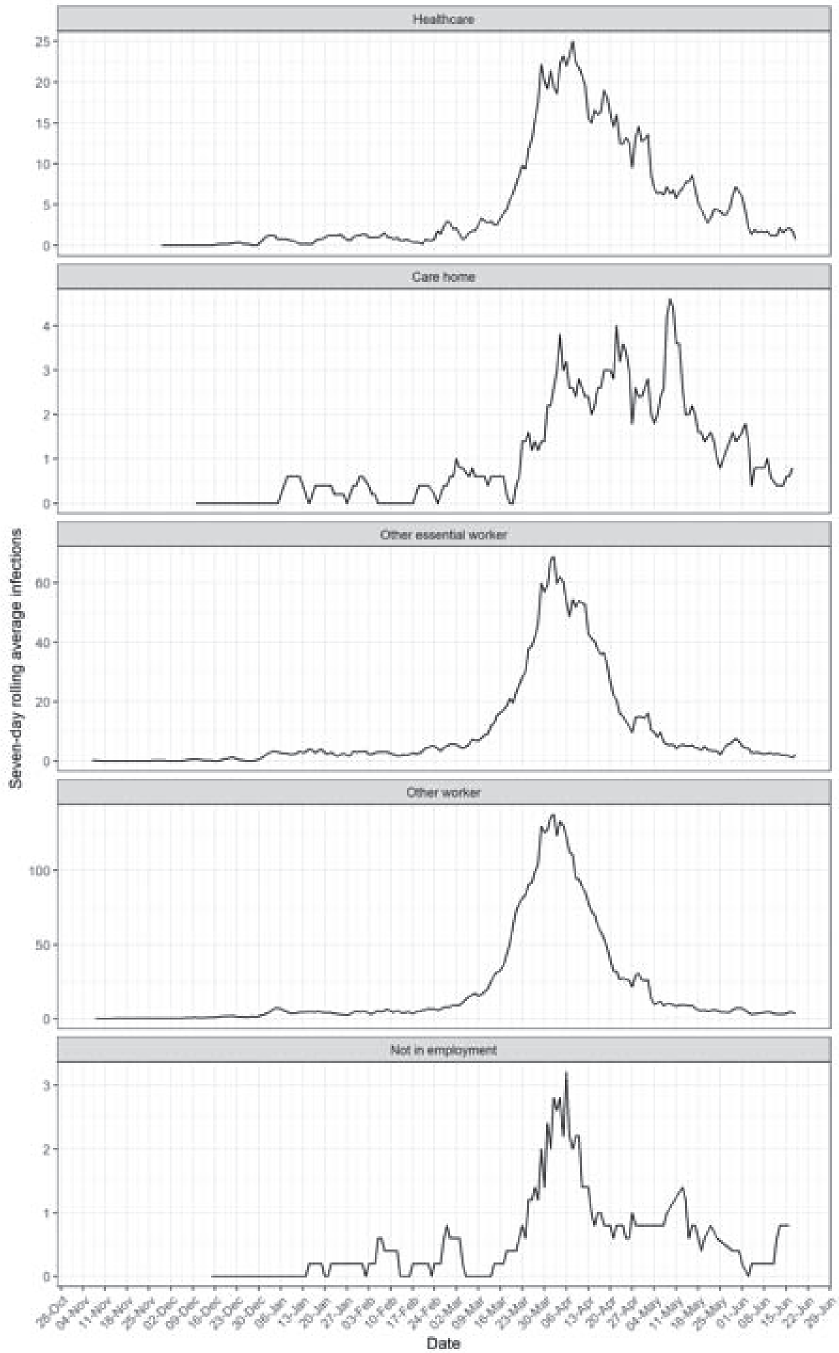
Legend: Scatterplot for each lower tier local authority showing change in prevalence from round 1 to round 2 (left) and round 2 to round 3 (right). The dashed line represents no change, the blue line the linear regression. The slope of the fitted line indicates the average decrease in prevalence, and the scatter shows the variation, with some areas seeing an increase and others a very large decrease between rounds.

Figure 4 Epidemic curve reconstructed from reported date of onset from 17,576 IgG antibody positive people, by round of study



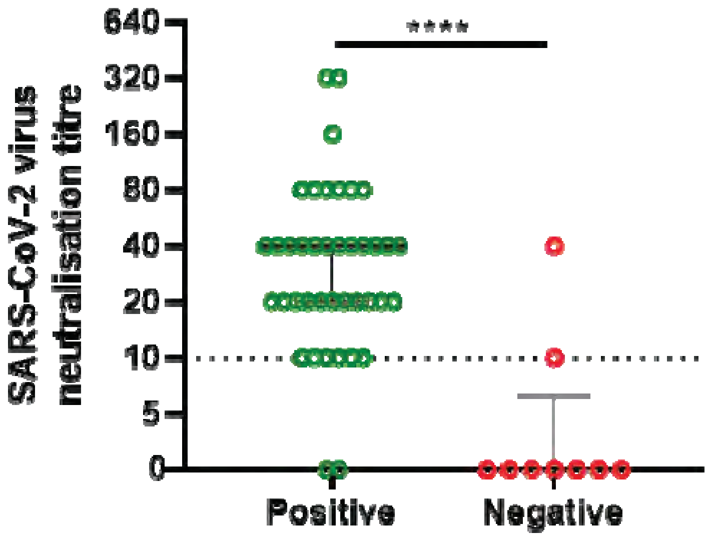
Legend: Seven-day rolling average of number of infections (by onset date) in 17,576 participants testing positive for antibodies and who reported a date of onset for symptoms of COVID19, shown separately for each round, together with an arrow indicating the date of the national lockdown in England (March 23rd 2020).

Figure 5 Epidemic curve reconstructed from reported date of onset from all three rounds by employment type, to June 2020



Legend: Seven-day rolling average of number of infections (by onset date) in participants testing positive for antibodies and who reported a date of onset for symptoms of COVID19 by employment type. Healthcare worker includes those with and without direct patient contact; care home worker includes those with and without direct client contact; other essential worker as defined by the UK Government https://www.gov.uk/guidance/coronavirus-covid-19-getting-tested#essential-workers includes those in emergency services, essential public services, transport and education; other worker includes workers not working in health or social care or on the UK Government list of essential workers.`

Figure 6: Association of LFIA result with virus microneutralisation titre in 49 healthcare workers with PCR-confirmed SARS-CoV-2 infection



Human serum samples were assayed by live virus neutralisation assay and tested by Fortress LFT. Median virus neutralisation titres are shown and Mann-Whitney test shows a significant difference (P<0.0001) between the neutralisation titres of those which were positive (n=40) and those which were negative (n=9) by LFT

Table 1: Prevalence of antibody positivity to SARS-CoV-2 using LFIA test over three study rounds from June to September

	Total antibody positive	*Total tests (with valid results)*	*Crude prevalence % [95% CI]*	*Adjusted & weighted[1] prevalence % [95% CI]*
Round 1 (20 Jun - 13 July)	5544	99908	5.55 [5.41-5.69]	5.96 [5.78-6.14]
Round 2 (31 Jul – 13 Aug)	4995	105829	4.72 [4.59-4.85]	4.83 [4.67-5.00]
Round 3 (15 - 28 Sept)	7037	159367	4.42 [4.32-4.52]	4.38 [4.25-4.51]

Legend: Adjusted for test characteristics, weighted to the age, sex, region, ethnicity, index of multiple deprivation of England population (see Supplementary Appendix for detail on weighting)

Table 2: Change in prevalence of antibody positivity to SARS-CoV-2 using LFIA test over three rounds from June to September

	ROUND 1			ROUND 2			ROUND 3			COMPARISONS		
Category	Total antibody positive	Total tests (with valid results)	Prevalence R1 (weighted and adjusted where appropriate)	Total antibody positive	Total tests (with valid results)	Prevalence R2 (weighted and adjusted where appropriate)	Total antibody positive	Total tests (with valid results)	Prevalence R3 (weighted and adjusted where appropriate)	% difference R1/R2	% difference R2/R3	% difference R1/R3
Full cohort**												
England	5544	99908	5.96 [5.78-6.14]	4995	105829	4.83 [4.67-5.00]	7037	159367	4.38 [4.25-4.51]	-18.96 [-21.81, -16.11]	-9.11 [-12.01, -6.21]	-26.34 [-28.86, -23.83]
Sex**												
Male	2405	43825	6.17 [5.91-6.44]	2117	46269	4.87 [4.64-5.11]	3029	69421	4.37 [4.19-4.56]	-21.07 [-24.96, -17.18]	-10.27 [-14.58, -5.95]	-29.17 [-32.74, -25.61]
Female	3139	56083	5.75 [5.50-6.01]	2878	59560	4.79 [4.57-5.03]	4008	89944	4.39 [4.21-4.57]	-16.70 [-20.87, -12.52]	-8.56 [-12.73, -4.38]	-23.83 [-27.48, -20.17]
Age**												
18-24	463	6499	7.86 [7.26-8.50]	411	6493	7.31 [6.75-7.90]	574	8763	6.70 [6.25-7.17]	-7.12 [-14.50, 0.25]	-8.34 [-15.32, -1.37]	-14.89 [-21.63, -8.14]
25-34	930	13366	7.83 [7.35-8.32]	775	13573	5.88 [5.47-6.32]	1036	20212	5.15 [4.83-5.49]	-24.90 [-30.52, -19.28]	-12.24 [-18.54, -5.95]	-34.10 [-39.21, -28.99]
35-44	964	17052	6.09 [5.65-6.56]	837	17130	5.12 [4.71-5.55]	1202	26687	4.60 [4.28-4.94]	-16.09 [-23.15, -9.03]	-10.16 [-17.38, -2.93]	-24.63 [-31.03, -18.23]
45-54	1255	20634	6.41 [5.98-6.87]	1100	21487	5.48 [5.08-5.90]	1559	32403	4.96 [4.65-5.29]	-14.51 [-21.06, -7.96]	-9.49 [-16.06, -2.92]	-22.62 [-28.55, -16.69]
55-64	1131	20404	5.92 [5.46-6.40]	1074	21840	4.70 [4.30-5.14]	1537	32870	4.33 [4.01-4.67]	-20.61 [-27.87, -13.34]	-7.66 [-15.53, 0.21]	-26.69 [-33.45, -19.93]
65-74	568	15543	3.16 [2.76-3.59]	594	17617	2.74 [2.37-3.14]	787	26542	2.25 [1.96-2.56]	-13.61 [-25.95, -1.27]	-17.52 [-29.93, -5.11]	-28.80 [-39.87, -17.72]
75+	233	6410	3.31 [2.86-3.79]	204	7689	1.61 [1.26-2.00]	342	11890	2.01 [1.70-2.34]	-51.06 [-63.44, -38.67]	24.84 [3.73, 45.96]	-38.97 [-50.76, -27.19]
Region**												
North East	196	3574	5.03 [4.30-5.85]	202	4027	4.34 [3.66-5.10]	296	6327	3.87 [3.33-4.46]	-13.92 [-28.43, 0.60]	-10.83 [-25.35, 3.69]	-23.26 [-36.38, -10.14]
North West	714	11996	6.65 [6.14-7.19]	657	12995	5.25 [4.80-5.74]	910	18616	4.50 [4.15-4.87]	-21.05 [-28.42, -13.68]	-14.10 [-21.90, -6.29]	-32.18 [-38.80, -25.56]
Yorkshire and The Humber	284	6519	3.95 [3.46-4.48]	306	7391	3.97 [3.50-4.49]	399	10594	3.37 [3.01-3.77]	0.76 [-11.65, 13.16]	-15.37 [-26.20, -4.53]	-14.68 [-25.82, -3.54]
East Midlands	601	12684	4.23 [3.71-4.80]	533	13685	3.37 [2.90-3.89]	756	20469	3.11 [2.73-3.52]	-20.33 [-32.39, -8.27]	-7.72 [-20.77, 5.34]	-26.48 [-37.35, -15.60]

West Midlands	547	9620	5.82 [5.28-6.40]	592	10062	6.97 [6.41-7.57]	672	15046	4.77 [4.37-5.19]	19.93 [10.31, 29.55]	-31.71 [-38.74, -24.68]	-18.04 [-26.29, -9.79]
East of England	805	14433	5.09 [4.59-5.63]	689	15189	4.02 [3.58-4.50]	993	23174	3.69 [3.34-4.07]	-20.83 [-30.26, -11.39]	-8.21 [-18.41, 1.99]	-27.31 [-35.95, -18.66]
London	1045	9547	12.96 [12.34-13.59]	855	9872	9.38 [8.86-9.93]	1265	15227	9.46 [9.03-9.91]	-27.55 [-31.94, -23.15]	0.75 [-4.37, 5.86]	-27.01 [-31.10, -22.92]
South East	995	21979	3.92 [3.54-4.32]	891	22632	3.09 [2.75-3.45]	1325	34738	3.01 [2.74-3.30]	-21.43 [-30.61, -12.24]	-2.27 [-12.30, 7.77]	-23.21 [-31.63, -14.80]
South West	357	9556	2.79 [2.37-3.25]	270	9976	1.28 [0.95-1.65]	421	15176	1.62 [1.34-1.94]	-54.48 [-68.46, -40.50]	27.34 [2.34, 52.34]	-41.94 [-55.20, -28.67]
Employment												
Healthcare (patient-facing)	379	3402	12.91 [11.61-14.32]	389	3511	13.15 [11.87-14.52]	578	5416	13.37 [12.33-14.47]	1.70 [-8.37, 11.77]	1.75 [-7.15, 10.65]	3.49 [-5.73, 12.70]
Healthcare (other)	73	1151	6.84 [5.15-8.91]	62	1112	5.27 [3.74-7.20]	113	1692	7.39 [5.95-9.07]	-22.95 [-48.54, 2.63]	40.23 [9.87, 70.59]	8.04 [-16.52, 32.60]
Care home (client-facing)	115	761	19.56 [16.42-23.10]	83	727	14.46 [11.67-17.72]	108	979	11.09 [8.96-13.59]	-26.02 [-41.87, -10.17]	-23.24 [-41.36, -5.12]	-43.20 [-57.52, -28.89]
Care home (other)	12	146	9.02 [4.53-16.26]	12	224	3.63 [1.13-8.16]	23	257	18.16 [13.28-24.23]	-59.76 [-110.98, -8.54]	400.28 [277.96, 522.59]	101.33 [40.47, 162.20]
Other essential worker	1209	19927	6.63 [6.21-7.07]	1019	19615	5.23 [4.85-5.64]	1463	29572	4.93 [4.62-5.25]	-21.12 [-27.15, -15.08]	-5.74 [-12.43, 0.96]	-25.64 [-31.22, -20.06]
Other worker	2189	37855	6.50 [6.20-6.82]	1982	40782	5.17 [4.90-5.44]	2704	60731	4.35 [4.14-4.56]	-20.62 [-24.92, -16.31]	-15.86 [-20.50, -11.22]	-33.23 [-37.23, -29.23]
Not in employment	1516	35737	4.18 [3.92-4.45]	1412	39030	3.38 [3.15-3.63]	1988	59369	3.10 [2.91-3.29]	-18.90 [-24.64, -13.16]	-8.58 [-14.79, -2.37]	-25.84 [-31.10, -20.57]
Resident in a care home												
Yes	6	131	3.83 [0.86-9.92]	18	259	6.69 [3.66-11.23]	25	348	6.97 [4.23-10.83]	74.67 [-27.94, 177.28]	4.04 [-47.09, 55.16]	81.72 [-15.67, 179.11]
No	5538	99777	5.00 [4.83-5.17]	4977	105570	3.99 [3.84-4.15]	7012	159019	3.63 [3.51-3.75]	-20.20 [-23.40, -17.00]	-9.02 [-12.53, -5.51]	-27.40 [-30.20, -24.60]
Ethnicity[1]**												
White	4827	92737	5.01 [4.83-5.19]	4384	98003	4.05 [3.89-4.22]	6176	148227	3.63 [3.50-3.76]	-19.16 [-22.55, -15.77]	-10.37 [-14.07, -6.67]	-27.54 [-30.74, -24.35]
Mixed	106	1347	8.92 [7.09-11.08]	76	1308	6.19 [4.66-8.05]	108	1865	5.69 [4.46-7.16]	-30.61 [-50.78, -10.43]	-7.92 [-31.99, 16.16]	-36.10 [-54.71, -17.49]
Asian	369	3658	11.86 [10.99-12.77]	340	3930	11.23 [10.40-12.10]	439	5518	9.70 [9.06-10.38]	-5.31 [-12.48, 1.85]	-13.62 [-20.21, -7.03]	-18.21 [-24.70, -11.72]
Black	135	900	17.34 [15.75-19.05]	102	936	11.92 [10.56-13.42]	154	1304	13.77 [12.56-15.06]	-31.26 [-39.91, -22.61]	15.52 [4.53, 26.51]	-20.59 [-28.78, -12.40]
Other	79	762	12.28 [10.21-14.66]	70	939	8.25 [6.50-10.33]	98	1393	8.25 [6.77-9.95]	-32.82 [-49.27, -16.37]	-0.12 [-20.85, 20.61]	-32.90 [-48.21, -17.59]
IMD quintile [2]**												
Most deprived: 1	682	10082	7.28 [6.84-7.74]	639	10997	6.27 [5.86-6.69]	827	15681	5.39 [5.08-5.71]	-13.87 [-19.64, -8.10]	-14.04 [-19.78, -8.29]	-25.96 [-31.18, -20.74]

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2	947	16015	6.43 [6.03-6.85]	855	16973	5.35 [4.98-5.73]	1183	25206	4.82 [4.53-5.12]	-16.80 [-22.71, -10.89]	-9.91 [-16.07, -3.74]	-25.04 [-30.48, -19.60]
3	1196	21474	5.87 [5.48-6.29]	1027	23231	4.46 [4.12-4.82]	1518	34548	4.37 [4.09-4.66]	-24.19 [-30.49, -17.89]	-2.02 [-8.97, 4.93]	-25.72 [-31.52, -19.93]
4	1287	24840	5.22 [4.84-5.62]	1182	25979	4.25 [3.91-4.61]	1678	39595	3.84 [3.57-4.12]	-18.58 [-25.48, -11.69]	-9.65 [-16.94, -2.35]	-26.44 [-32.76, -20.11]
Least deprived: 5	1432	27497	4.99 [4.61-5.39]	1292	28649	3.85 [3.52-4.21]	1831	44337	3.51 [3.24-3.78]	-22.65 [-29.86, -15.43]	-9.09 [-16.88, -1.30]	-29.66 [-36.27, -23.05]
Household size												
1	720	15052	4.08 [3.68-4.50]	671	16777	3.13 [2.79-3.50]	953	24735	2.96 [2.67-3.25]	-23.04 [-32.11, -13.97]	-5.75 [-15.97, 4.47]	-27.45 [-36.03, -18.87]
2	1784	36413	4.22 [3.95-4.49]	1593	39252	3.20 [2.97-3.44]	2273	59922	2.88 [2.70-3.07]	-24.17 [-30.09, -18.25]	-10.00 [-16.56, -3.44]	-31.75 [-36.97, -26.54]
3	1158	19734	5.38 [5.00-5.79]	1065	20898	4.45 [4.10-4.82]	1484	31429	4.00 [3.73-4.29]	-17.29 [-24.16, -10.41]	-10.34 [-17.30, -3.37]	-25.84 [-31.97, -19.70]
4	1204	19611	5.71 [5.32-6.13]	1077	20110	4.77 [4.40-5.15]	1549	30208	4.49 [4.20-4.80]	-16.46 [-23.12, -9.81]	-5.87 [-12.79, 1.05]	-21.37 [-27.50, -15.24]
5	447	6403	6.72 [6.00-7.51]	392	6174	5.96 [5.26-6.73]	529	9354	5.13 [4.58-5.71]	-11.31 [-22.02, -0.60]	-13.93 [-24.66, -3.19]	-23.66 [-33.33, -13.99]
6	152	1848	8.22 [6.82-9.84]	124	1822	6.51 [5.23-8.02]	162	2575	5.89 [4.84-7.10]	-20.80 [-38.08, -3.53]	-9.68 [-28.73, 9.37]	-28.47 [-44.28, -12.65]
7+	79	827	9.82 [7.63-12.47]	73	796	9.36 [7.18-12.02]	87	1130	7.59 [5.88-9.64]	-4.68 [-28.62, 19.25]	-18.91 [-41.45, 3.63]	-22.71 [-44.09, -1.32]
Population density quintile												
1	808	19779	3.24 [2.91-3.58]	680	20253	2.36 [2.07-2.67]	964	30655	2.10 [1.87-2.34]	-27.16 [-36.73, -17.59]	-11.02 [-22.03, 0.00]	-35.19 [-43.83, -26.54]
2	1002	19514	4.50 [4.14-4.88]	894	20060	3.68 [3.35-4.04]	1275	30773	3.31 [3.04-3.58]	-17.78 [-25.56, -10.00]	-10.60 [-18.75, -2.45]	-26.44 [-33.56, -19.33]
3	1026	19817	4.55 [4.19-4.93]	929	20090	3.88 [3.55-4.25]	1258	30350	3.31 [3.04-3.58]	-14.73 [-22.42, -7.03]	-14.95 [-22.68, -7.22]	-27.47 [-34.51, -20.44]
4	1145	20094	5.18 [4.80-5.58]	950	20101	4.01 [3.66-4.37]	1404	29967	3.96 [3.68-4.25]	-22.59 [-29.54, -15.64]	-1.25 [-8.98, 6.48]	-23.55 [-29.92, -17.18]
5	1563	20704	7.41 [6.98-7.85]	1542	25325	5.65 [5.30-6.01]	2136	37622	5.15 [4.88-5.44]	-23.75 [-29.01, -18.49]	-8.67 [-14.16, -3.19]	-30.36 [-35.22, -25.51]
COVID history[3]												
Positive test	277	341	96.18 [90.78-100.00]	274	361	89.76 [84.13-94.73]	478	754	74.69 [70.48-78.74]	-6.67 [-11.89, -1.46]	-16.78 [-21.95, -11.61]	-22.33 [-26.98, -17.69]
Suspected by doctor	353	1144	35.49 [32.35-38.79]	348	1214	32.85 [29.87-35.99]	470	1811	29.58 [27.21-32.07]	-7.41 [-16.03, 1.21]	-9.98 [-18.20, -1.77]	-16.65 [-24.49, -8.82]
Suspected by respondent	3118	17893	19.31 [18.65-19.99]	2742	16914	17.85 [17.19-18.52]	3867	27546	15.23 [14.74-15.73]	-7.61 [-10.98, -4.25]	-14.62 [-17.82, -11.43]	-21.13 [-24.08, -18.18]
No	1698	80390	0.86 [0.74-0.98]	1565	87217	0.48 [0.37-0.58]	2144	129126	0.31 [0.23-0.40]	-45.35 [-58.14, -32.56]	-33.33 [-52.08, -14.58]	-63.95 [-75.58, -52.33]
Symptom category[4]												

No symptoms	1791	81150	0.97 [0.85-1.10]	1636	87971	0.55 [0.45-0.66]	2267	130438	0.41 [0.32-0.49]	-44.33 [-55.67, -32.99]	-25.45 [-41.82, -9.09]	-58.76 [-69.07, -48.45]
Atypical symptoms only	347	3426	10.52 [9.35-11.79]	294	3185	9.43 [8.28-10.71]	469	5108	9.38 [8.46-10.37]	-10.36 [-21.58, 0.86]	-0.64 [-11.88, 10.60]	-10.93 [-21.10, -0.76]
Screening symptoms	3406	15332	25.08 [24.29-25.88]	3065	14673	23.48 [22.70-24.28]	4301	23821	20.07 [19.48-20.66]	-6.4 [-9.4, -3.3]	-14.5 [-17.4, -11.6]	-20.0 [-22.7, -17.3]
COVID contacts[5]												
Yes, with confirmed case	742	3946	20.97 [19.54-22.47]	753	4543	18.28 [17.01-19.62]	1107	7793	15.43 [14.52-16.38]	-12.78 [-19.22, -6.34]	-15.59 [-21.61, -9.57]	-26.37 [-32.09, -20.65]
Yes, with suspected case	896	5307	18.65 [17.47-19.90]	842	5115	18.15 [16.95-19.40]	1121	7362	16.66 [15.69-17.67]	-2.73 [-9.12, 3.65]	-8.15 [-14.10, -2.20]	-10.67 [-16.46, -4.88]
No	3906	90655	3.50 [3.35-3.67]	3400	96171	2.57 [2.43-2.72]	4809	144211	2.33 [2.22-2.44]	-26.57 [-30.86, -22.29]	-9.73 [-14.40, -5.06]	-33.71 [-37.43, -30.00]

Legend: Adjusted and weighted (marked **, see Supplementary Appendix for methods) prevalence for each round by sociodemographic and clinical factors for each round of the study. Final columns show the percentage change (95% confidence limits) between R1 and R2, R2 and R3, and R1 and R3.

[1] Ethnicity categories: Asian includes Asian (south, east) and Asian British; Black includes Black African, Caribbean, Black British;

[2] Based on Index of Multiple Deprivation (2019) at lower super output area;

[3] COVID History is self-reported, based on response to the question, "Before you took this antibody test, did you think you had had COVID-19?" with response options of Yes, confirmed by a positive test (swab/*PCR/antigen test); Yes, suspected by a doctor but not tested; Yes, my own suspicions; No.

[4] Symptom category is constructed from responses about self-reported specific symptoms. These were grouped into those reporting one or more "screening symptoms" based on recommendations for having a SARS-CoV-2 test (new persistent cough, fever, loss of sense of smell or taste), or atypical (any other symptom(s)), or none.

[5] Self reported contact with a case of COVID19

AR-00890

Delay or Avoidance of Medical Care Because of COVID-19–Related Concerns — United States, June 2020

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Temporary disruptions in routine and nonemergency medical care access and delivery have been observed during periods of considerable community transmission of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19) (*1*). However, medical care delay or avoidance might increase morbidity and mortality risk associated with treatable and preventable health conditions and might contribute to reported excess deaths directly or indirectly related to COVID-19 (*2*). To assess delay or avoidance of urgent or emergency and routine medical care because of concerns about COVID-19, a web-based survey was administered by Qualtrics, LLC, during June 24–30, 2020, to a nationwide representative sample of U.S. adults aged ≥18 years. Overall, an estimated 40.9% of U.S. adults have avoided medical care during the pandemic because of concerns about COVID-19, including 12.0% who avoided urgent or emergency care and 31.5% who avoided routine care. The estimated prevalence of urgent or emergency care avoidance was significantly higher among the following groups: unpaid caregivers for adults* versus noncaregivers (adjusted prevalence ratio [aPR] = 2.9); persons with two or more selected underlying medical conditions† versus those without those conditions (aPR = 1.9); persons with health insurance versus those without health insurance (aPR = 1.8); non-Hispanic Black (Black) adults (aPR = 1.6) and Hispanic or Latino (Hispanic) adults (aPR = 1.5) versus non-Hispanic White (White) adults; young adults aged 18–24 years versus adults aged 25–44 years (aPR = 1.5); and persons with disabilities§ versus those without disabilities (aPR = 1.3). Given this widespread reporting of medical care avoidance because of COVID-19 concerns, especially among persons at increased risk for severe COVID-19, urgent efforts are warranted to ensure delivery of services that, if deferred, could result in patient harm. Even during the COVID-19 pandemic, persons experiencing a medical emergency should seek and be provided care without delay (*3*).

During June 24–30, 2020, a total of 5,412 (54.7%) of 9,896 eligible adults¶ completed web-based COVID-19 Outbreak Public Evaluation Initiative surveys administered by Qualtrics, LLC.** The Human Research Ethics Committee of Monash University (Melbourne, Australia) reviewed and approved the study protocol on human subjects research.

* Unpaid caregiver status was self-reported. The definition of an unpaid caregiver for adults was having provided unpaid care to a relative or friend aged ≥18 years to help them take care of themselves at any time in the last 3 months. Examples provided to survey respondents included helping with personal needs, household chores, health care tasks, managing a person's finances, taking them to a doctor's appointment, arranging for outside services, and visiting regularly to see how they are doing.

† Selected underlying medical conditions known to increase the risk for severe COVID-19 included in this analysis were obesity (body mass index [BMI] ≥30 kg/m²), diabetes, high blood pressure, cardiovascular disease, and any type of cancer. BMI was calculated from self-reported height and weight as BMI = weight (lb)/[height (in)]^2 x 703 (https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html). The remaining conditions were assessed using the following question: "Have you ever been diagnosed with any of the following conditions?" with the following four response options: 1) "Never"; 2) "Yes, I have in the past, but don't have it now"; 3) "Yes I have, but I do not regularly take medications or receive treatment"; and 4) "Yes I have, and I am regularly taking medications or receiving treatment." Respondents who answered that they have been diagnosed and chose either response 3 or 4 were considered as having the specified medical condition.

§ Persons who had a disability were defined as such based on a qualifying response to either one of two questions: "Are you limited in any way in any activities because of physical, mental, or emotional condition?" and "Do you have any health conditions that require you to use special equipment, such as a cane, wheelchair, special bed, or special telephone?" https://www.cdc.gov/brfss/questionnaires/pdf-ques/2015-brfss-questionnaire-12-29-14.pdf.

¶ Eligibility to complete a survey during June 24–30, 2020, was determined following electronic contact of potential participants based on a minimum age of 18 years and residence within the United States. Age and residence were assessed using screening questions without indication of eligibility criteria before commencement of the earliest survey (recontacted respondents: April 2–8, 2020; first-time respondents: June 24–30, 2020). Residence was reassessed among recontacted respondents during June 24–30, and one respondent whose primary residence had changed to outside of the United States was excluded from the analysis. Country-specific geolocation verification via IP address mapping was used to ensure respondents were responding from the United States. Informed consent was obtained electronically during June 24–30, 2020, before enrollment into the study as a participant. All surveys underwent Qualtrics, LLC data quality screening procedures, including algorithmic and keystroke analysis for attention patterns, click-through behavior, duplicate responses, machine responses, and inattentiveness. Respondents who failed an attention or speed check, along with any responses that failed data quality screening procedures, were excluded from the analysis (6.6%).

** The COVID-19 Outbreak Public Evaluation (COPE) Initiative (www.thecopeinitiative.org) is designed to assess public attitudes, behaviors, and beliefs related to the coronavirus disease 2019 (COVID-19) pandemic, and to evaluate the mental and physical health consequences of the pandemic. The COPE Initiative surveys included in this analysis were administered by Qualtrics, LLC (https://www.qualtrics.com/), a commercial survey company with a network of participant pools comprising hundreds of suppliers and with varying recruitment methodologies that include digital advertisements and promotions, word-of-mouth and membership referrals, social networks, television and radio advertisements, and offline mail-based approaches.

This activity was also reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[††] Respondents were informed of the study purposes and provided electronic consent before commencement, and investigators received anonymized responses. The 5,412 participants included 3,683 (68.1%) first-time respondents and 1,729 (31.9%) persons who had completed a related survey[§§] during April 2–8, 2020. Among the 5,412 participants, 4,975 (91.9%) provided complete data for all variables in this analysis. Quota sampling and survey weighting[¶¶] were employed to improve cohort representativeness of the U.S. population by gender, age, and race/ethnicity.

Respondents were asked “Have you delayed or avoided medical care due to concerns related to COVID-19?” Delay or avoidance was evaluated for emergency (e.g., care for immediate life-threatening conditions), urgent (e.g., care for immediate non–life-threatening conditions), and routine (e.g., annual check-ups) medical care. Given the potential for variation in interpretation of whether conditions were life-threatening, responses for urgent and emergency care delay or avoidance were combined for analysis. Covariates included gender; age; race/ethnicity; disability status; presence of one or more selected underlying medical conditions known to increase risk for severe COVID-19; education; essential worker status***; unpaid adult caregiver status; U.S. census region; urban/rural classification[†††]; health insurance status; whether respondents knew someone who had received a positive SARS-CoV-2 test result or had died from COVID-19; and whether the respondents believed they were at high risk for severe COVID-19. Comparisons within all these subgroups were evaluated using multivariable Poisson regression models[§§§] with robust standard errors to estimate prevalence ratios adjusted for all covariates, 95% confidence intervals, and p-values to evaluate statistical significance (α = 0.05) using the R survey package (version 3.29) and R software (version 4.0.2; The R Foundation).

†† 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

§§ https://www.medrxiv.org/content/10.1101/2020.04.22.20076141v1.

¶¶ Statistical raking and weight trimming were employed to improve the cross-sectional June cohort representativeness of the U.S. population by gender, age, and race/ethnicity according to the 2010 U.S. Census.

*** Essential worker status was self-reported. For the aPRs, essential workers were compared with all other respondents (including those who were nonessential workers, retired, unemployed, and students).

††† Rural-urban classification was determined by using self-reported ZIP codes according to the Federal Office of Rural Health Policy definition of rurality. https://www.hrsa.gov/rural-health/about-us/definition/datafiles.html.

§§§ Reference groups were chosen for ease of interpretation. For example, the household income level of $50,000–$99,999 was selected as the reference group because the median household income was $61,937 in the United States in 2018. https://www.census.gov/content/dam/Census/library/publications/2019/acs/acsbr18-01.pdf.

As of June 30, 2020, among 4,975 U.S. adult respondents, 40.9% reported having delayed or avoided any medical care, including urgent or emergency care (12.0%) and routine care (31.5%), because of concerns about COVID-19 (Table 1). Groups of persons among whom urgent or emergency care avoidance exceeded 20% and among whom any care avoidance exceeded 50% included adults aged 18–24 years (30.9% for urgent or emergency care; 57.2% for any care), unpaid caregivers for adults (29.8%; 64.3%), Hispanic adults (24.6%; 55.5%), persons with disabilities (22.8%; 60.3%), persons with two or more selected underlying medical conditions (22.7%; 54.7%), and students (22.7%; 50.3%). One in four unpaid caregivers reported caring for adults who were at increased risk for severe COVID-19.

In the multivariable Poisson regression models, differences within groups were observed for urgent or emergency care avoidance (Figure) and any care avoidance (Table 2). Adjusted prevalence of urgent or emergency care avoidance was significantly higher among unpaid caregivers for adults versus noncaregivers (2.9; 2.3–3.6); persons with two or more selected underlying medical conditions versus those without those conditions (1.9; 1.5–2.4); persons with health insurance versus those without health insurance (1.8; 1.2–2.8); Black adults (1.6; 1.3–2.1) and Hispanic adults (1.5; 1.2–2.0) versus White adults; young adults aged 18–24 years versus adults aged 25–44 years (1.5; 1.2–1.8); and persons with disabilities versus those without disabilities (1.3; 1.1–1.5). Avoidance of urgent or emergency care was significantly lower among adults aged ≥45 years than among younger adults.

Discussion

As of June 30, 2020, an estimated 41% of U.S. adults reported having delayed or avoided medical care during the pandemic because of concerns about COVID-19, including 12% who reported having avoided urgent or emergency care. These findings align with recent reports that hospital admissions, overall emergency department (ED) visits, and the number of ED visits for heart attack, stroke, and hyperglycemic crisis have declined since the start of the pandemic (*3*–*5*), and that excess deaths directly or indirectly related to COVID-19 have increased in 2020 versus prior years (*2*). Nearly one third of adult respondents reported having delayed or avoided routine medical care, which might reflect adherence to community mitigation efforts such as stay-at-home orders, temporary closures of health facilities, or additional factors. However, if routine care avoidance were to be sustained, adults could miss opportunities for management of chronic conditions, receipt of routine vaccinations, or early detection of new conditions, which might worsen outcomes.

TABLE 1. Estimated prevalence of delay or avoidance of medical care because of concerns related to COVID-19, by type of care and respondent characteristics — United States, June 30, 2020

		Type of medical care delayed or avoided*					
		Urgent or emergency		Routine		Any	
Characteristic	No. (%)†	%†	P-value§	%†	P-value§	%†	P-value§
All respondents	**4,975 (100)**	**12.0**	—	**31.5**	—	**40.9**	—
Gender							
Female	2,528 (50.8)	11.7	0.598	35.8	<0.001	44.9	<0.001
Male	2,447 (49.2)	12.3		27.0		36.7	
Age group, yrs							
18–24	650 (13.1)	30.9	<0.001	29.6	0.072	57.2	<0.001
25–44	1,740 (35.0)	14.9		34.2		44.8	
45–64	1,727 (34.7)	5.7		30.0		34.5	
≥65	858 (17.3)	4.4		30.3		33.5	
Race/Ethnicity							
White, non-Hispanic	3,168 (63.7)	6.7	<0.001	30.9	0.020	36.2	<0.001
Black, non-Hispanic	607 (12.2)	23.3		29.7		48.1	
Asian, non-Hispanic	238 (4.8)	8.6		31.3		37.7	
Other race or multiple races, non-Hispanic¶	150 (3.0)	15.5		23.9		37.3	
Hispanic, any race or races	813 (16.3)	24.6		36.4		55.5	
Disability**							
Yes	1,108 (22.3)	22.8	<0.001	42.9	<0.001	60.3	<0.001
No	3,867 (77.7)	8.9		28.2		35.3	
Underlying medical condition††							
No	2,537 (51.0)	8.2	<0.001	27.9	<0.001	34.7	<0.001
One	1,328 (26.7)	10.4		33.0		41.2	
Two or more	1,110 (22.3)	22.7		37.7		54.7	
2019 household income, USD							
<25,000	665 (13.4)	13.9	0.416	31.2	0.554	42.8	0.454
25,000–49,999	1,038 (20.9)	11.1		30.9		38.6	
50,000–99,999	1,720 (34.6)	12.5		30.5		41.1	
≥100,000	1,552 (31.2)	11.2		33.0		41.4	
Education							
Less than high school diploma	65 (1.3)	15.6	0.442	24.7	0.019	37.9	0.170
High school diploma	833 (16.7)	12.3		28.1		38.1	
Some college	1,302 (26.2)	13.6		29.7		40.3	
Bachelor's degree	1,755 (35.3)	11.2		34.8		43.6	
Professional degree	1,020 (20.5)	10.9		31.2		39.5	
Employment status							
Employed	3,049 (61.3)	14.6	<0.001	31.5	0.407	43.3	<0.001
Unemployed	630 (12.7)	8.7		34.4		39.5	
Retired	1,129 (22.7)	5.3		29.9		33.8	
Student	166 (3.3)	22.7		30.5		50.3	
Essential worker status§§							
Essential worker	1,707 (34.3)	19.5	<0.001	32.4	0.293	48.0	<0.001
Nonessential worker	1,342 (27.0)	8.4		30.3		37.3	
Unpaid caregiver status¶¶							
Unpaid caregiver for adults	1,344 (27.0)	29.8	<0.001	41.0	<0.001	64.3	<0.001
Not unpaid caregiver for adults	3,631 (73.0)	5.4		27.9		32.2	
U.S. Census region***							
Northeast	1,122 (22.6)	11.0	0.008	33.9	0.203	42.5	0.460
Midwest	936 (18.8)	8.5		32.0		38.7	
South	1,736 (34.9)	13.9		29.6		40.7	
West	1,181 (23.7)	13.0		31.5		41.5	
Rural/Urban classification†††							
Urban	4,411 (88.7)	12.3	0.103	31.5	0.763	41.2	0.216
Rural	564 (11.3)	9.4		30.9		38.2	
Health insurance status							
Yes	4,577 (92.0)	12.4	0.036	32.6	<0.001	42.3	<0.001
No	398 (8.0)	7.8		18.4		24.8	
Know someone with positive test results for SARS-CoV-2§§§							
Yes	989 (19.9)	8.8	0.004	40.7	<0.001	46.6	<0.001
No	3,986 (80.1)	12.8		29.2		39.5	

See table footnotes on the next page.

AR-00893

TABLE 1. (*Continued*) Estimated prevalence of delay or avoidance of medical care because of concerns related to COVID-19, by type of care and respondent characteristics — United States, June 30, 2020

		Type of medical care delayed or avoided*					
		Urgent or emergency		Routine		Any	
Characteristic	No. (%)†	%†	P-value§	%†	P-value§	%†	P-value§
Knew someone who died from COVID-19							
Yes	364 (7.3)	10.1	0.348	41.4	<0.001	46.3	0.048
No	4,611 (92.7)	12.2		30.7		40.5	
Believed to be in group at high risk for severe COVID-19							
Yes	981 (19.7)	10.0	0.050	42.5	<0.001	49.4	<0.001
No	3,994 (80.3)	12.5		28.8		38.8	

Abbreviations: CI = confidence interval; COVID-19 = coronavirus disease 2019; USD = U.S. dollars.

* The types of medical care avoidance are not mutually exclusive; respondents had the option to indicate that they had delayed or avoided more than one type of medical care (i.e., routine medical care and urgent/emergency medical care).

† Statistical raking and weight trimming were employed to improve the cross-sectional June cohort representativeness of the U.S. population by gender, age, and race/ethnicity according to the 2010 U.S. Census.

§ The Rao-Scott adjusted Pearson chi-squared test was used to test for differences in observed and expected frequencies among groups by characteristic for avoidance of each type of medical care (e.g., whether avoidance of routine medical care differs significantly by gender). Statistical significance was evaluated at a threshold of $\alpha = 0.05$.

¶ "Other" race includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, or Other.

** Persons who had a disability were defined as such based on a qualifying response to either one of two questions: "Are you limited in any way in any activities because of physical, mental, or emotional condition?" and "Do you have any health conditions that require you to use special equipment, such as a cane, wheelchair, special bed, or special telephone?" https://www.cdc.gov/brfss/questionnaires/pdf-ques/2015-brfss-questionnaire-12-29-14.pdf.

†† Selected underlying medical conditions known to increase the risk for severe COVID-19 included in this analysis were obesity, diabetes, high blood pressure, cardiovascular disease, and any type of cancer. Obesity is defined as body mass index ≥30 kg/m^2 and was calculated from self-reported height and weight (https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html). The remaining conditions were assessed using the question "Have you ever been diagnosed with any of the following conditions?" with response options of 1) "Never"; 2) "Yes, I have in the past, but don't have it now"; 3) "Yes I have, but I do not regularly take medications or receive treatment"; and 4) "Yes I have, and I am regularly taking medications or receiving treatment." Respondents who answered that they have been diagnosed and chose either response 3 or 4 were considered as having the specified medical condition.

§§ Essential worker status was self-reported.

¶¶ Unpaid caregiver status was self-reported. Unpaid caregivers for adults were defined as having provided unpaid care to a relative or friend aged ≥18 years at any time in the last 3 months. Examples provided to survey respondents included helping with personal needs, household chores, health care tasks, managing a person's finances, taking them to a doctor's appointment, arranging for outside services, and visiting regularly to see how they are doing.

*** Region classification was determined by using the U.S. Census Bureau's Census Regions and Divisions. https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf.

††† Rural-urban classification was determined by using self-reported ZIP codes according to the Federal Office of Rural Health Policy definition of rurality. https://www.hrsa.gov/rural-health/about-us/definition/datafiles.html.

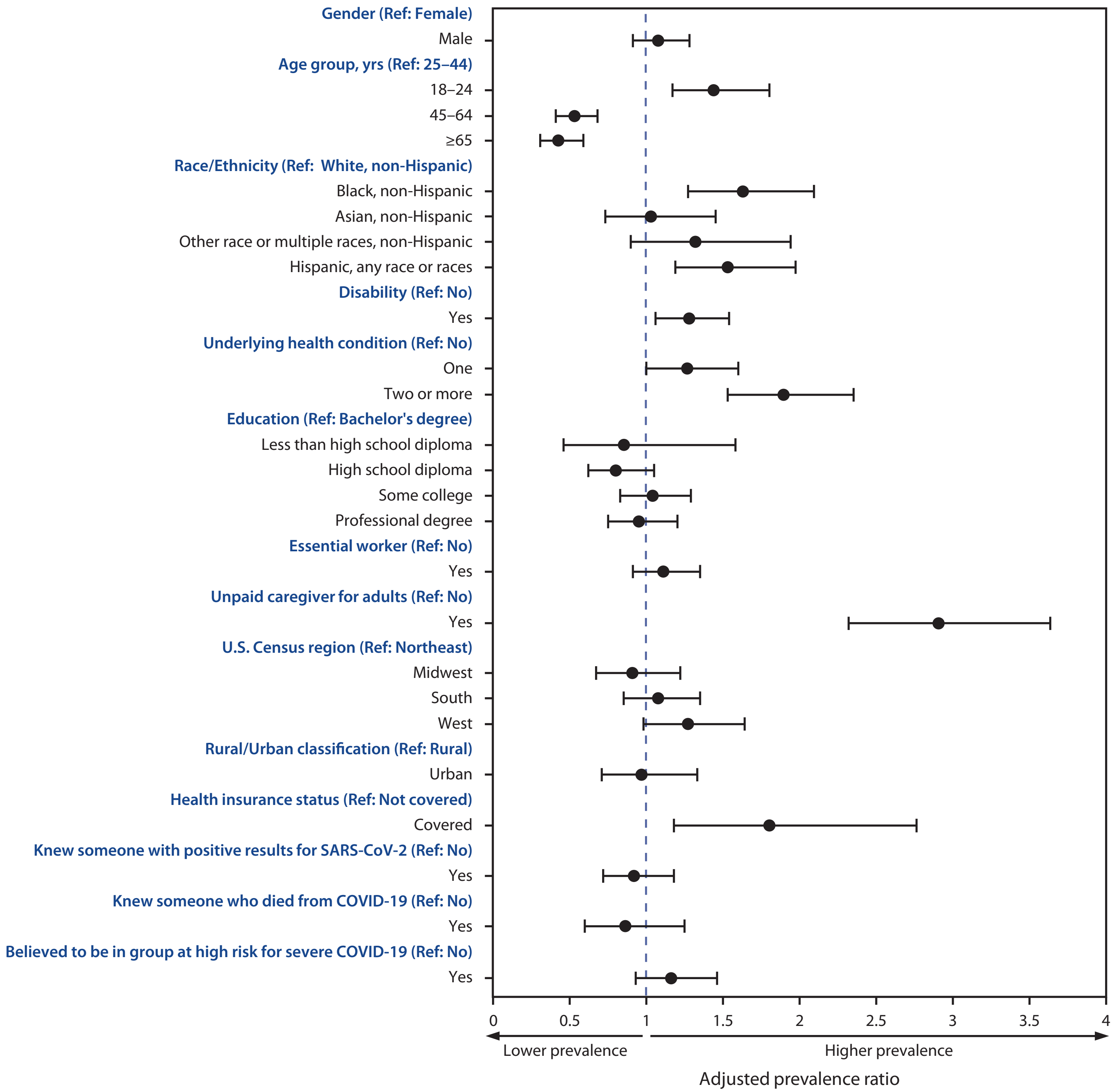
§§§ For this question, respondents were asked to select the following statement, if applicable: "I know someone who has tested positive for COVID-19."

Avoidance of both urgent or emergency and routine medical care because of COVID-19 concerns was highly prevalent among unpaid caregivers for adults, respondents with two or more underlying medical conditions, and persons with disabilities. For caregivers who reported caring for adults at increased risk for severe COVID-19, concern about exposure of care recipients might contribute to care avoidance. Persons with underlying medical conditions that increase their risk for severe COVID-19 (*6*) are more likely to require care to monitor and treat these conditions, potentially contributing to their more frequent report of avoidance. Moreover, persons at increased risk for severe COVID-19 might have avoided health care facilities because of perceived or actual increased risk of exposure to SARS-CoV-2, particularly at the onset of the pandemic. However, health care facilities are implementing important safety precautions to reduce the risk of SARS-CoV-2 infection among patients and personnel. In contrast, delay or avoidance of care might increase risk for life-threatening medical emergencies. In a recent study, states with large numbers of COVID-19–associated deaths also experienced large proportional increases in deaths from other underlying causes, including diabetes and cardiovascular disease (*7*). For persons with disabilities, accessing medical services might be challenging because of disruptions in essential support services, which can result in adverse health outcomes. Medical services for persons with disabilities might also be disrupted because of reduced availability of accessible transportation, reduced communication in accessible formats, perceptions of SARS-CoV-2 exposure risk, and specialized needs that are difficult to address with routine telehealth delivery during the pandemic response. Increasing accessibility of medical and telehealth services¶¶¶ might help prevent delay of needed care.

Increased prevalences of reported urgent or emergency care avoidance among Black adults and Hispanic adults compared with White adults are especially concerning given increased COVID-19-associated mortality among Black adults and Hispanic adults (*8*). In the United States, the age-adjusted COVID-19 hospitalization rates are approximately five times higher among Black persons and four times higher among Hispanic persons than are those among White

¶¶¶ https://www.cdc.gov/coronavirus/2019-ncov/hcp/telehealth.html.

FIGURE. Adjusted prevalence ratios*,† for characteristics§,¶,,†† associated with delay or avoidance of urgent or emergency medical care because of concerns related to COVID-19 — United States, June 30, 2020**



Abbreviation: COVID-19 = coronavirus disease 2019.

* Comparisons within subgroups were evaluated using Poisson regressions used to calculate a prevalence ratio adjusted for all characteristics shown in figure.

† 95% confidence intervals indicated with error bars.

§ "Other" race includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, or Other.

¶ Selected underlying medical conditions known to increase the risk for severe COVID-19 were obesity, diabetes, high blood pressure, cardiovascular disease, and any type of cancer. Obesity is defined as body mass index ≥30 kg/m^2 and was calculated from self-reported height and weight (https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html). The remaining conditions were assessed using the question "Have you ever been diagnosed with any of the following conditions?" with response options of 1) "Never"; 2) "Yes, I have in the past, but don't have it now"; 3) "Yes I have, but I do not regularly take medications or receive treatment"; and 4) "Yes I have, and I am regularly taking medications or receiving treatment." Respondents who answered that they have been diagnosed and chose either response 3 or 4 were considered as having the specified medical condition.

** Essential worker status was self-reported. For the adjusted prevalence ratios, essential workers were compared with all other respondents (including those who were nonessential workers, retired, unemployed, and students).

†† Unpaid caregiver status was self-reported. Unpaid caregivers for adults were defined as having provided unpaid care to a relative or friend aged ≥18 years to help them take care of themselves at any time in the last 3 months.

TABLE 2. Characteristics associated with delay or avoidance of any medical care because of concerns related to COVID-19 — United States, June 30, 2020

Characteristic	Weighted* no.	Avoided or delayed any medical care aPR†	(95% CI†)	P-value†
All respondents	**4,975**	—	—	—
Gender				
Female	2,528	Referent	—	—
Male	2,447	0.81	(0.75–0.87)§	<0.001
Age group, yrs				
18–24	650	1.12	(1.01–1.25)§	0.035
25–44	1,740	Referent	—	—
45–64	1,727	0.80	(0.72–0.88)§	<0.001
≥65	858	0.72	(0.64–0.81)§	<0.001
Race/Ethnicity				
White, non-Hispanic	3,168	Referent	—	—
Black, non-Hispanic	607	1.07	(0.96–1.19)	0.235
Asian, non-Hispanic	238	1.04	(0.91–1.18)	0.567
Other race or multiple races, non-Hispanic¶	150	0.87	(0.71–1.07)	0.196
Hispanic, any race or races	813	1.15	(1.03–1.27)§	0.012
Disability**				
Yes	1,108	1.33	(1.23–1.43)§	<0.001
No	3,867	Referent	—	—
Underlying medical condition††				
No	2,537	Referent	—	—
One	1,328	1.15	(1.05–1.25)§	0.004
Two or more	1,110	1.31	(1.20–1.42)§	<0.001
Education				
Less than high school diploma	65	0.72	(0.53–0.98)§	0.037
High school diploma	833	0.79	(0.71–0.89)§	<0.001
Some college	1,302	0.85	(0.78–0.93)§	0.001
Bachelor's degree	1,755	Referent	—	—
Professional degree	1,020	0.90	(0.82–0.98)§	0.019
Essential workers vs others§§				
Essential workers	1,707	1.00	(0.92–1.09)	0.960
Other respondents (nonessential workers, retired persons, unemployed persons, and students)	3,268	Referent	—	—
Unpaid caregiver status¶¶				
Unpaid caregiver for adults	1,344	1.64	(1.52–1.78)§	<0.001
Not unpaid caregiver for adults	3,631	Referent	—	—
U.S. Census region***				
Northeast	1,122	Referent	—	—
Midwest	936	0.93	(0.83–1.04)	0.214
South	1,736	0.90	(0.82–0.99)§	0.028
West	1,181	0.99	(0.89–1.09)	0.808

See table footnotes on the next page.

persons (*9*). Factors contributing to racial and ethnic disparities in SARS-CoV-2 exposure, illness, and mortality might include long-standing structural inequities that influence life expectancy, including prevalence and underlying medical conditions, health insurance status, and health care access and utilization, as well as work and living circumstances, including use of public transportation and essential worker status. Communities, health care systems, and public health agencies can foster equity by working together to ensure access to information, testing, and care to assure maintenance and management of physical and mental health.

The higher prevalence of medical care delay or avoidance among respondents with health insurance versus those without insurance might reflect differences in medical care-seeking behaviors. Before the pandemic, persons without insurance sought medical care much less frequently than did those with insurance (*10*), resulting in fewer opportunities for medical care delay or avoidance.

The findings in this report are subject to at least five limitations. First, self-reported data are subject to recall, response, and social desirability biases. Second, the survey did not assess reasons for COVID-19–associated care avoidance, such as adherence to public health recommendations; closure of health care provider facilities; reduced availability of public transportation; fear of exposure to infection with SARS-CoV-2; or availability, accessibility, and acceptance or recognition of

TABLE 2. (*Continued*) Characteristics associated with delay or avoidance of any medical care because of concerns related to COVID-19 — United States, June 30, 2020

Characteristic	Weighted* no.	Avoided or delayed any medical care aPR†	(95% CI†)	P-value†
Rural/Urban classification†††				
Urban	4,411	1.00	(0.89–1.12)	0.993
Rural	564	Referent	—	—
Health insurance status				
Yes	4,577	1.61	(1.31–1.98)§	<0.001
No	398	Referent	—	—
Know someone with positive test results for SARS-CoV-2§§§				
Yes	989	1.22	(1.12–1.33)§	<0.001
No	3,986	Referent	—	—
Knew someone who died from COVID-19				
Yes	364	0.99	(0.88–1.12)	0.860
No	4,611	Referent	—	—
Believed to be in a group at high risk for severe COVID-19				
Yes	981	1.33	(1.23–1.44)§	<0.001
No	3,994	Referent	—	—

Abbreviations: aPR = adjusted prevalence ratio; CI = confidence interval; COVID-19 = coronavirus disease 2019.

* Statistical raking and weight trimming were employed to improve the cross-sectional June cohort representativeness of the U.S. population by gender, age, and race/ethnicity according to the 2010 U.S. Census.

† Comparisons within subgroups were evaluated using Poisson regressions used to calculate a prevalence ratio adjusted for all characteristics listed, as well as a 95% CI and p-value. Statistical significance was evaluated at a threshold of $\alpha = 0.05$.

§ P-value calculated using Poisson regression among respondents within a characteristic is statistically significant at levels of $p<0.05$.

¶ "Other" race includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, or Other.

** Persons who had a disability were defined based on a qualifying response to either one of two questions: "Are you limited in any way in any activities because of physical, mental, or emotional condition?" and "Do you have any health conditions that require you to use special equipment, such as a cane, wheelchair, special bed, or special telephone?" https://www.cdc.gov/brfss/questionnaires/pdf-ques/2015-brfss-questionnaire-12-29-14.pdf.

†† Underlying medical conditions were obesity, diabetes, high blood pressure, cardiovascular disease, and any type of cancer. Obesity is defined as body mass index ≥30 kg/m^2 and was calculated from self-reported height and weight (https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html). The remaining conditions were assessed using the question "Have you ever been diagnosed with any of the following conditions?" with response options of 1) "Never"; 2) "Yes, I have in the past, but don't have it now"; 3) "Yes I have, but I do not regularly take medications or receive treatment"; and 4) "Yes I have, and I am regularly taking medications or receiving treatment." Respondents who answered that they have been diagnosed and chose either response 3 or 4 were considered as having the specified medical condition.

§§ Essential worker status was self-reported. For the adjusted prevalence ratios, essential workers were compared with all other respondents (including those who were nonessential workers, retired, unemployed, and students).

¶¶ Unpaid caregiver status was self-reported. Unpaid caregivers for adults were defined as having provided unpaid care to a relative or friend aged ≥18 years at any time in the last 3 months. Examples provided to survey respondents included helping with personal needs, household chores, health care tasks, managing a person's finances, taking them to a doctor's appointment, arranging for outside services, and visiting regularly to see how they are doing.

*** Region classification was determined by using the U.S. Census Bureau's Census Regions and Divisions. https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf.

††† Rural/urban classification was determined by using self-reported ZIP codes according to the Federal Office of Rural Health Policy definition of rurality. https://www.hrsa.gov/rural-health/about-us/definition/datafiles.html.

§§§ For this question, respondents were asked to select the following statement, if applicable: "I know someone who has tested positive for COVID-19."

telemedicine as a means of providing care in lieu of in-person services. Third, the survey did not assess baseline patterns of care-seeking or timing or duration of care avoidance. Fourth, perceptions of whether a condition was life-threatening might vary among respondents. Finally, although quota sampling methods and survey weighting were employed to improve cohort representativeness, this web-based survey might not be fully representative of the U.S. population for income, educational attainment, and access to technology. However, the findings are consistent with reported declines in hospital admissions and ED visits during the pandemic (*3–5*).

CDC has issued guidance to assist persons at increased risk for severe COVID-19 in staying healthy and safely following treatment plans**** and to prepare health care facilities to safely deliver care during the pandemic.†††† Additional public outreach in accessible formats tailored for diverse audiences might encourage these persons to seek necessary care. Messages could highlight the risks of delaying needed care, especially among persons with underlying medical conditions, and the importance of timely emergency care. Patient concerns related to potential exposure to SARS-CoV-2 in health care settings could be addressed by describing facilities' precautions to reduce exposure risk.

**** https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

†††† https://www.cdc.gov/coronavirus/2019-ncov/hcp/us-healthcare-facilities.html.

Summary

What is already known about this topic?

Delayed or avoided medical care might increase morbidity and mortality associated with both chronic and acute health conditions.

What is added by this report?

By June 30, 2020, because of concerns about COVID-19, an estimated 41% of U.S. adults had delayed or avoided medical care including urgent or emergency care (12%) and routine care (32%). Avoidance of urgent or emergency care was more prevalent among unpaid caregivers for adults, persons with underlying medical conditions, Black adults, Hispanic adults, young adults, and persons with disabilities.

What are the implications for public health practice?

Understanding factors associated with medical care avoidance can inform targeted care delivery approaches and communication efforts encouraging persons to safely seek timely routine, urgent, and emergency care.

Further exploration of underlying reasons for medical care avoidance is needed, including among persons with disabilities, persons with underlying health conditions, unpaid caregivers for adults, and those who face structural inequities. If care were avoided because of concern about SARS-CoV-2 exposure or if there were closures or limited options for in-person services, providing accessible telehealth or in-home health care could address some care needs. Even during the COVID-19 pandemic, persons experiencing a medical emergency should seek and be provided care without delay (*3*).

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Delayed and Forgone Health Care for Nonelderly Adults during the COVID-19 Pandemic

Findings from the September 11–28 Coronavirus Tracking Survey

Dulce Gonzalez, Michael Karpman, Genevieve M. Kenney, and Stephen Zuckerman

February 2021

The COVID-19 pandemic has disrupted health care in an unprecedented way, leading some patients to postpone or forgo care (Czeisler et al. 2020).[1] Visits to primary care physicians, emergency rooms, and other health care providers fell as providers scaled back their operations and patients curbed their health care use because of the pandemic (Garcia et al. 2020; Hartnett et al. 2020; Jiang et al. 2020; Mast and Munoz del Rio 2020; Mehrotra et al. 2020; Santoli et al. 2020). Most health care providers have new safety protocols in place[2] and have seen visits rebound since the start of the pandemic (Mehrotra et al. 2020). However, significant numbers of patients continue avoiding care because they fear exposure to the novel coronavirus (Morning Consult and American College of Emergency Physicians 2020),[3] and reduced patient volumes are leading some physicians to close their practices for financial reasons.[4]

Though some missed care may have been of low value or unnecessary, physicians report concern over unmet needs for care, particularly for people with chronic health conditions, whose health can deteriorate rapidly without careful monitoring and treatment.[5] Mortality data suggest the pandemic has caused a surge in excess deaths from conditions such as diabetes, dementia, hypertension, heart disease, and stroke, and a record number of drug overdose deaths occurred in the 12 months ending in May 2020 (Woolf et al. 2020).[6] These events underscore the importance of ensuring people with chronic physical and behavioral health conditions continue to access the care they need during the public health crisis and beyond.

Using data from the most recent wave of the Coronavirus Tracking Survey, a nationally representative survey of nonelderly adults conducted September 11 through 28, 2020, we examine delayed or forgone health care during the pandemic among adults ages 18 to 64. We examine experiences with nine types of health care services and assess patterns by race/ethnicity, income, and the presence of physical and mental health conditions, including conditions associated with elevated risk for severe illness from COVID-19.[7] Our analysis focuses on reported instances of delayed or forgone care resulting from patients' and providers' efforts to prevent transmission of the virus: (1) care respondents did not receive because they were worried about exposure to the coronavirus and (2) care they did not receive because a health care provider limited services because of the coronavirus outbreak.

Adults who reported not getting one or more types of care were asked whether they eventually got care (delayed care) or had still not gotten it at the time of the survey (forgone care). Because reported impacts of delaying care did not meaningfully differ from reported impacts of not getting care at all, we present estimates of delayed or forgone care in combination. In this analysis, we do not focus on delayed or forgone care for other reasons, such as lack of insurance, costs or affordability, preexisting provider shortages, or administrative barriers (e.g., prior authorization).[8] Though several surveys have quantified the prevalence of delayed or forgone care during the pandemic,[9] few have explored the extent for individual types of care, the experiences of adults with chronic health conditions (Czeisler et al. 2020), or how people say delaying or not getting care has affected their health, ability to work, and other routine activities.

We find the following:

- As of September 2020, more than one in three adults (36.0 percent) reported delaying or forgoing health care because of worry about exposure to the coronavirus or because a health care provider limited services during the pandemic. Black adults were more likely than white or Hispanic/Latinx[i] adults to report delaying or forgoing care (39.7 versus 34.3 percent and 35.5 percent) and more likely to report delaying or forgoing multiple types of care (28.5 versus 21.1 percent and 22.3 percent).
- About 4 in 10 adults with one or more chronic health conditions (40.7 percent) and more than half of adults with both a physical and mental health condition (56.3 percent) reported delaying or forgoing health care because of the pandemic. About 43.8 percent of the latter group delayed or went without multiple types of care. Adults with mental health conditions were at particularly high risk of delaying or forgoing care (52.0 percent).
- Dental care was the most common type of care adults delayed or did not receive because of the pandemic (25.3 percent of adults reported going without or delaying dental care), followed

[i] We use "Hispanic/Latinx" throughout this brief to reflect the different ways in which people self-identify. The US Census Bureau uses the term "Hispanic." The terms "white" and "Black" refer to adults who do not identify as Hispanic or Latinx.

by seeing a general doctor or specialist (20.6 percent) or receiving preventive health screenings or medical tests (15.5 percent).

- More than three-quarters of adults with delayed or forgone health care (76 percent) had one or more chronic health conditions, such as hypertension, diabetes, respiratory illness, heart disease, cancer, kidney disease, and mental health disorders.
- Among adults reporting delayed or forgone health care, almost one in three (32.6 percent) reported doing so worsened one or more of their health conditions or limited their abilities to work or perform other daily activities.

These results demonstrate the importance of addressing health issues that have not been attended to during the pandemic. Failing to do so could exacerbate health inequities by race and income and exacerbate health problems broadly, particularly among adults with mental health conditions.

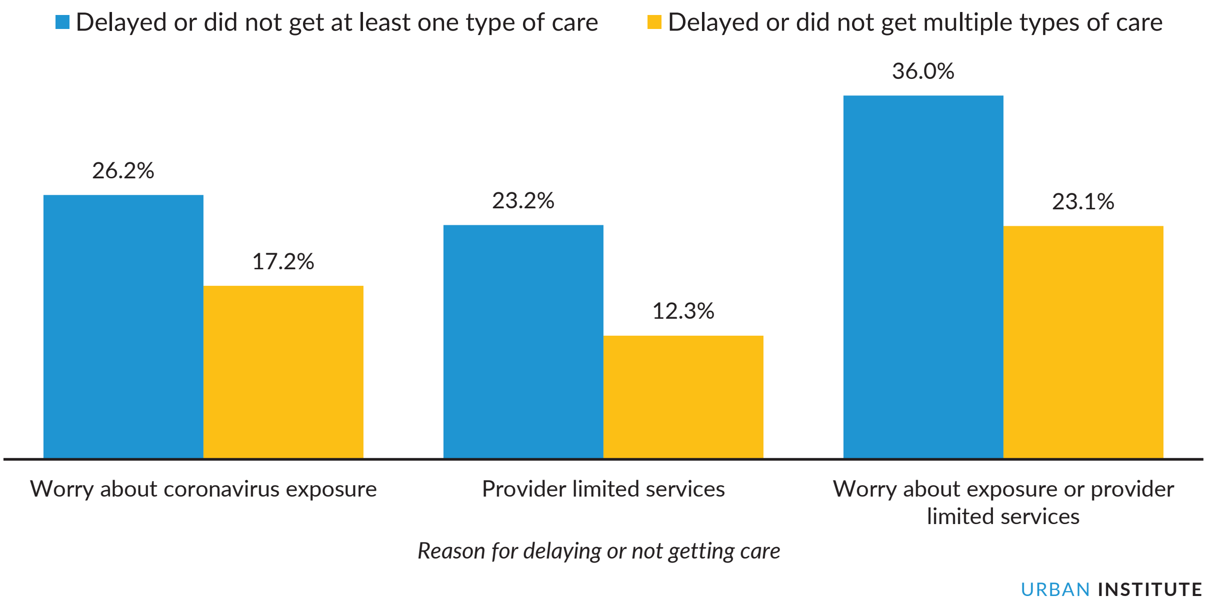
Results

As of September 2020, more than one in three adults (36.0 percent) reported delaying or forgoing health care because of worry about exposure to the coronavirus or because a health care provider limited services during the pandemic. Black adults were more likely than white or Hispanic/Latinx adults to report delaying or forgoing care (39.7 versus 34.3 percent and 35.5 percent) and more likely to report delaying or forgoing multiple types of care (28.5 versus 21.1 percent and 22.3 percent).

Overall, 36.0 percent of nonelderly adults delayed or not did not get at least one type of health care during the pandemic because of worry about exposure to coronavirus or because a provider limited services because of the pandemic. Nearly 1 in 4 (23.1 percent) adults reported delaying or forgoing multiple types of care for these reasons (figure 1). More than 1 in 4 (26.2 percent) reported delaying or forgoing care because of worries about exposure to the coronavirus, and more than 1 in 6 (17.2 percent) delayed or went without multiple types of care for this reason. Similar shares of adults delayed or did not get care because of providers limiting services: 23.2 percent delayed or did not get least one type of needed care and 12.3 percent delayed or did not get multiple types of care for this reason. More than 1 in 10 (11.8 percent) adults reported only delaying care, and nearly 1 in 4 (24.1 percent) did not get at least one type of care for pandemic-related reasons (data not shown).

FIGURE 1

Share of Adults Ages 18 to 64 Who Reported Delaying or Forgoing Health Care Because of the Pandemic, September 2020



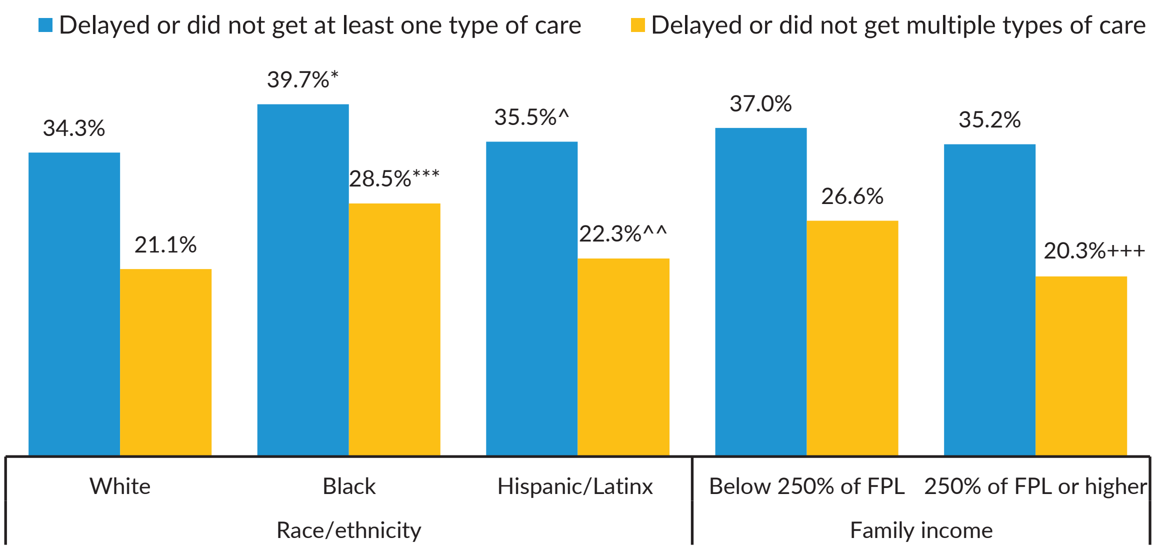
Source: Urban Institute Coronavirus Tracking Survey, wave 2, conducted September 11 through 28, 2020.

As noted, 39.7 percent of Black adults reported delaying or forgoing one or more types of care because they worried about exposure to the coronavirus or their providers had limited services because of the pandemic (figure 2). This share was higher than that for both white (34.3 percent) and Hispanic/Latinx (35.5 percent) adults. Black adults were also more likely to report delaying or forgoing multiple types of care (28.5 percent) than white (21.1 percent) and Hispanic/Latinx adults (22.3 percent). Adults with family incomes below 250 percent of the federal poverty level were more likely to report delaying or forgoing multiple types of care than adults with higher incomes (26.6 percent versus 20.3 percent).

Differences in delayed or forgone care by race/ethnicity and income were primarily driven by differences in avoiding care because of concerns about exposure to the virus: Black adults were more likely than white and Hispanic/Latinx adults to delay or forgo care for this reason, and adults with lower incomes were more likely to delay or forgo care for this reason than those with higher incomes (data not shown). We did not find statistically significant differences by race or ethnicity and income in delayed or forgone care because providers limited their services.

FIGURE 2

Share of Adults Ages 18 to 64 Who Reported Delaying or Forgoing Health Care Because of the Pandemic, by Race/Ethnicity and Family Income, September 2020



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Source: Urban Institute Coronavirus Tracking Survey, wave 2, conducted September 11 through 28, 2020.
Notes: FPL = federal poverty level. Estimates are not shown for non-Hispanic/Latinx adults who are not Black or white or are more than one race. Delayed or forgone health care is care not received because of worry about exposure to the coronavirus or because health care providers limited services because of the pandemic.
*/**/*** Estimate differs significantly from white adults at the 0.10/0.05/0.01 level, using two-tailed tests.
^/^^/^^^ Estimate differs significantly from Black adults at the 0.10/0.05/0.01 level, using two-tailed tests.
+/++/+++ Estimate differs significantly from adults with incomes below 250% of FPL at the 0.10/0.05/0.01 level, using two-tailed tests.

About 4 in 10 adults with one or more chronic health conditions (40.7 percent) and more than half of adults with both a physical and mental health condition (56.3 percent) reported delaying or forgoing health care because of the pandemic. About 43.8 percent of the latter group delayed or went without multiple types of care. Adults with mental health conditions were at particularly high risk of delaying or forgoing care (52.0 percent).

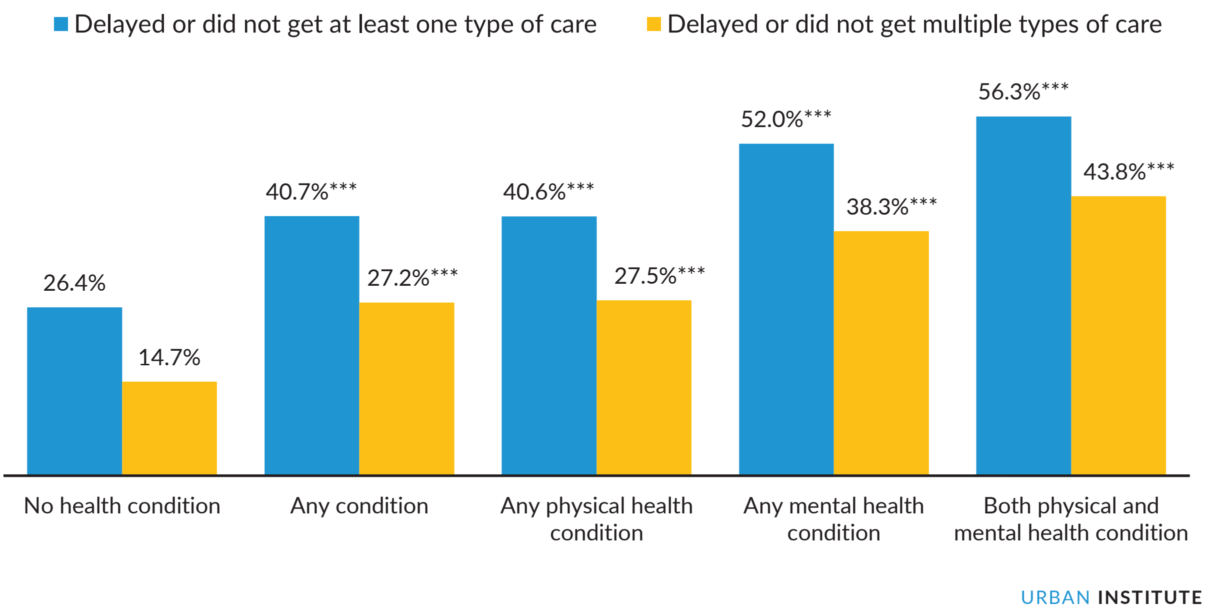
As shown in figure 3, adults with at least one chronic health condition were more likely than adults with no chronic conditions to have delayed or forgone care because of the pandemic (40.7 percent versus 26.4 percent). This pattern may reflect greater health care needs, heightened concerns about exposure to the coronavirus, or greater difficulty finding available providers among those with chronic health conditions. A person's likelihood of delaying or forgoing care increased with their number of chronic conditions: 32.7 percent of adults with one chronic condition and 45.5 percent of adults with multiple chronic conditions delayed or went without one or more types of care (data not shown).

Adults with both a physical and mental health condition reported delaying or forgoing care at particularly high rates; more than half (56.3 percent) delayed or went without one or more types of

care because of the pandemic, and 4 in 10 (43.8 percent) delayed or did not get multiple types of care. Though the presence of both physical and mental health conditions was associated with higher rates of delaying or forgoing needed health care, such rates were especially high among those with mental health conditions (52.0 percent).

FIGURE 3

Share of Adults Ages 18 to 64 Who Reported Delaying or Forgoing Health Care Because of the Pandemic, by Presence of Chronic Health Conditions, September 2020



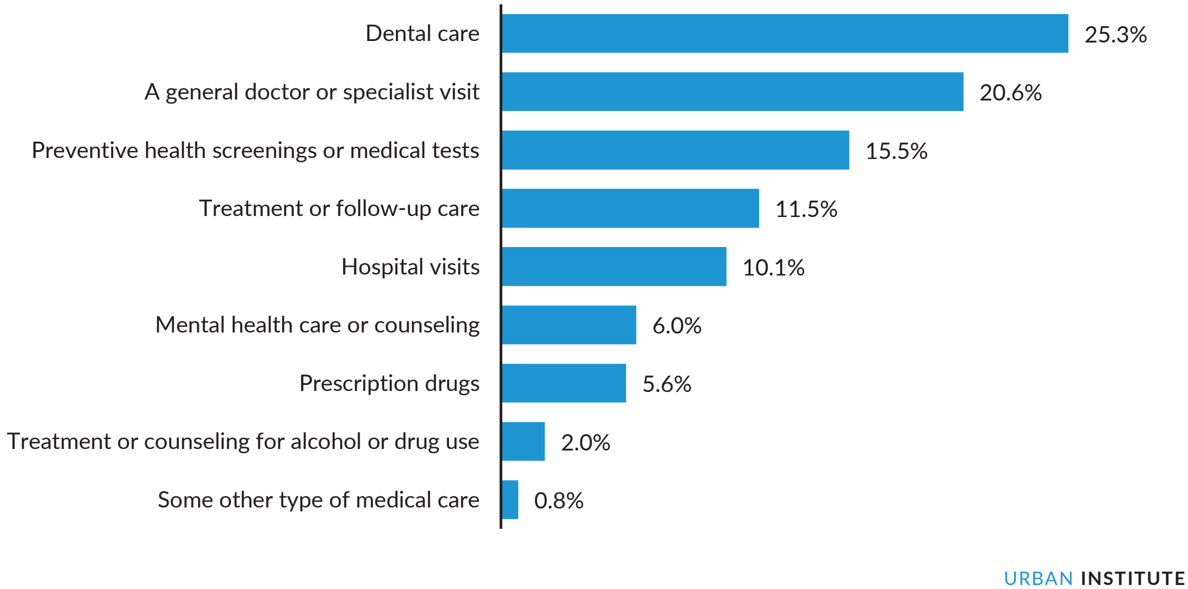
Source: Urban Institute Coronavirus Tracking Survey, wave 2, conducted September 11 through 28, 2020.
Notes: Delayed or forgone health care is care not received because of worry about exposure to the coronavirus or because health care providers limited services because of the pandemic.
*/**/*** Estimate differs significantly from adults without chronic health conditions at the 0.10/0.05/0.01 level, using two-tailed tests.

Dental care was the most common type of care adults delayed or did not receive because of the pandemic (25.3 percent), followed by seeing a general doctor or specialist (20.6 percent) or receiving preventive health screenings or medical tests (15.5 percent).

As noted above and in figure 4, dental care was the most common type of care adults delayed or did not receive because of the pandemic. Adults also delayed or did not get other types of care that may be important for managing chronic conditions and detecting and preventing disease: One in five (20.6 percent) reported not seeing a general doctor or specialist. Another 15.5 percent had a delayed or unmet need for preventive health screenings or medical tests, and 11.5 percent delayed or went without treatment or follow-up care. Some adults also reported not going to hospitals (10.1 percent) and delaying or not getting mental health care or counseling (6.0 percent), prescription drugs (5.6 percent), or treatment or counseling for alcohol or drug use (2.0 percent).

FIGURE 4

Types of Health Care Adults Ages 18 to 64 Delayed or Did Not Get Because of the Pandemic, September 2020



Source: Urban Institute Coronavirus Tracking Survey, wave 2, conducted September 11 through 28, 2020.
Notes: Delayed or forgone health care is care not received because of worry about exposure to the coronavirus or because health care providers limited services because of the pandemic.

More than three-quarters of adults with delayed or forgone health care (76.0 percent) had one or more chronic health conditions, such as hypertension, diabetes, respiratory illness, heart disease, cancer, and mental health disorders.

Those who delayed or did not get health care because of the pandemic were more than 15 percentage points more likely than those who did not delay or go without care to have a chronic condition (76.0 percent versus 62.3 percent; data not shown). As shown in table 1, the physical health conditions most commonly reported by adults with delayed or forgone care included obesity, high cholesterol, high blood pressure, arthritis, diabetes, asthma, chronic obstructive pulmonary disease and other respiratory illnesses, heart disease, and cancer. Mental health conditions such as anxiety and depressive disorders were twice as common among adults with delayed or forgone care as among adults who did not delay or go without care (36.4 percent versus 18.9 percent; data not shown).

TABLE 1

Presence of Chronic Health Conditions among Adults Ages 18 to 64 Delaying or Forgoing Health Care, September 2020

Chronic health conditions	Percent
Has a chronic health condition	**76.0**
Has a physical health condition	**67.9**
Obesity	34.7
High cholesterol	29.4
Hypertension	28.9
Some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia	20.5
Asthma	13.6
Diabetes (excluding gestational or prediabetes)	10.1
Chronic obstructive pulmonary disease, emphysema, or chronic bronchitis	4.9
Coronary heart disease, angina, heart attack, or other heart condition	4.9
Cancer	4.1
Chronic kidney disease	3.2
Stroke	2.0
Liver disease, including cirrhosis	2.0
Dementia, including Alzheimer's disease	0.9
Cystic or pulmonary fibrosis	0.8
Sickle cell disease or thalassemia	0.4
Has a mental health condition	**36.4**
Any type of anxiety disorder	28.4
Any type of depression	26.4
Any other type of mental health condition	8.5

Source: Urban Institute Coronavirus Tracking Survey, wave 2, conducted September 11 through 28, 2020.
Notes: *N* = 1,510 adults. Delayed or forgone health care is care not received because of worry about exposure to the coronavirus or because health care providers limited services because of the pandemic.

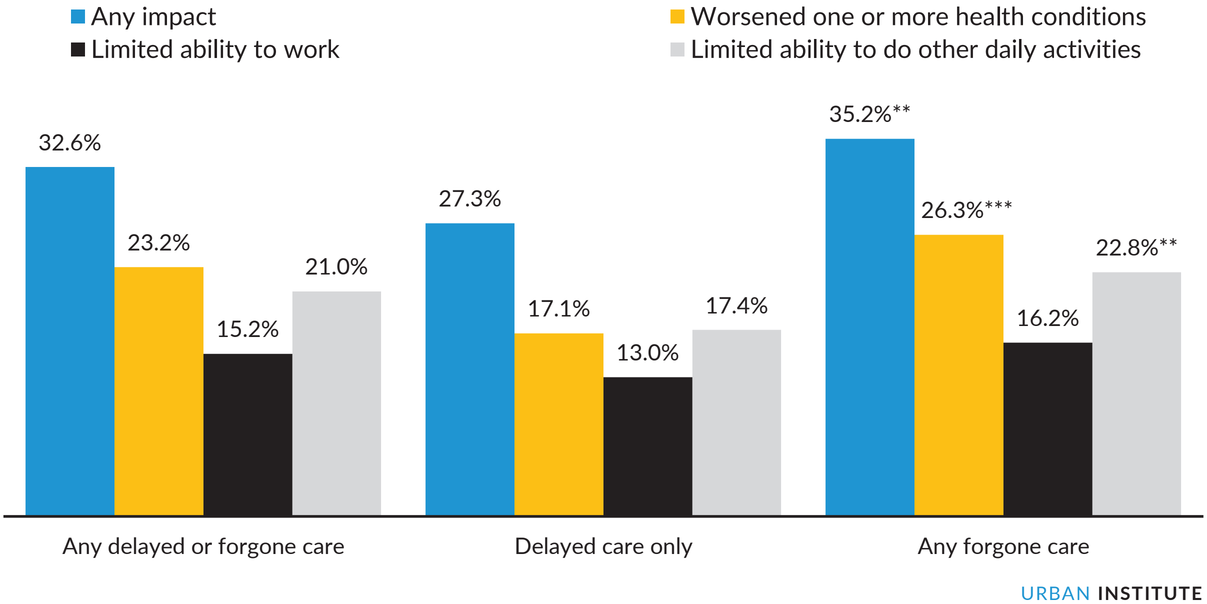
Among adults reporting delayed or forgone health care, almost one in three (32.6 percent) reported doing so worsened one or more of their health conditions or limited their abilities to work or perform other daily activities.

Figure 5 shows adults' reported impacts of delaying or forgoing care. An estimated 23.2 percent of these adults reported going without or delaying care worsened a health condition, 15.2 percent reported it limited their ability to work, and 21.0 percent reported it limited their ability to do other daily activities.

Adults who reported never getting at least one type of care were more likely to report experiencing these negative consequences than adults who only delayed care (35.2 percent versus 27.3 percent); they were more likely to report doing so worsened one of their health conditions (26.3 percent versus 17.1 percent) and limited their ability to do other daily activities (22.8 percent versus 17.4 percent). For adults who delayed or did without multiple types of care, we cannot link consequences to specific services. When we separate adults who only delayed or went without dental care, we find very few of these adults reported one or more of these adverse consequences. This suggests the consequences for health, work, and other daily activities differ depending on the type of care delayed or missed. We do not show these estimates because of sample size limitations.

FIGURE 5

Reported Impact of Delayed and Forgone Health Care among Adults Ages 18 to 64, September 2020



Source: Urban Institute Coronavirus Tracking Survey, wave 2, conducted September 11 through 28, 2020.
Notes: Delayed or forgone health care is care not received because of worry about exposure to the coronavirus or because health care providers limited services because of the pandemic.
*/**/*** Estimate differs significantly from adults who reported only delaying care because of the pandemic at the 0.10/0.05/0.01 level, using two-tailed tests.

Discussion

We find that, as of September 2020, 36 percent of nonelderly adults had delayed or gone without health care because of worry about exposure to the coronavirus or because a health care provider limited services because of the pandemic. Black adults reported forgoing or delaying care because of the pandemic at higher rates than white and Hispanic/Latinx adults, which suggests the pandemic is exacerbating existing racial health inequities. In addition, adults reported delaying or forgoing care that can be important for managing chronic conditions and detecting and preventing disease, such as general doctor or specialist visits, preventive health screenings and medical tests, and follow-up care.

We find adults with chronic conditions, particularly those with a mental health condition, were more likely to have delayed or gone without care than those without chronic health conditions. These patterns may reflect not only greater needs for care among people with chronic conditions but their greater fear of exposure to the coronavirus or greater difficulty finding providers. More than three-quarters of adults who delayed or did not get care because of the pandemic reported at least one of the chronic health conditions we examined, including conditions that place people at high risk for severe illness from COVID-19. Finally, nearly one in three adults who delayed or went without care reported it negatively affected their health, ability to work, or ability to perform other daily activities,

highlighting the detrimental ripple effects of delaying or forgoing care on overall health, functioning, and well-being.

Tackling unmet health care needs requires effectively assuaging fears about exposure to the coronavirus. Patients must be reassured that providers' safety precautions follow public health guidelines, and that these precautions effectively prevent transmission in offices, clinics, and hospitals. More data showing health care settings are not common sources of transmission and better communication with the public to promote the importance of seeking needed and routine care are also needed. Children have been missing care during the pandemic (Gonzalez et al. 2021), and Medicaid has been using available resources and promising strategies to address this (McMorrow et al. 2020). Similar strategies could be employed for adults. For example, Medicaid managed-care organizations could target outreach and case management services to patients who have chronic health issues but have been missing out on care or not getting recommended screenings. Our findings also highlight the importance of continued efforts to reduce COVID-19 transmission and promote vaccination to reduce patients' exposure to the virus.

With providers closing or limiting in-person services during the pandemic, our findings also underscore the importance of supporting telehealth, chronic disease self-management, and care coordination among providers. People with mental health conditions appear to be at particularly elevated risk of not getting care and could benefit from facilitated access to telehealth services. Telehealth use expanded greatly over the first six months of the pandemic, but not uniformly across the population. Another analysis of September 2020 Coronavirus Tracking Survey data showed that Black and Hispanic/Latinx adults were more likely than white adults to report having wanted a telehealth visit but not received one since the pandemic began, and that difficulties getting a telehealth visit were also more common among adults who were in poorer health or had chronic health conditions (Smith and Blavin 2021).[10] Much work remains to ensure all patients have equitable access to remote care during and after the pandemic.

Though this study does not focus on cost, it will likely be a barrier for many people who will be ready to return to health care settings when they feel safe. The pandemic has led to widespread negative economic impacts, and many of those most affected by the recession have also delayed or forgone care because of cost or COVID-19 concerns (Gonzalez et al. 2020). Enhanced efforts are needed to ensure all people have affordable insurance and access to care during and after the pandemic. Full recovery will also require shoring up provider capacity as demand for health care returns, including making additional funding available to ensure providers facing pandemic-related financial hardship can keep their practices open. And, health insurance coverage alone is not enough; policymakers will need to address other long-standing concerns like material hardship, financial instability, and language and cultural barriers that prevent even those with health insurance from equitable access to needed care (Berkowitz, Cené, and Chatterjee 2020).

Data and Methods

This brief uses data from the second wave of the Urban Institute's Coronavirus Tracking Survey, a nationally representative internet-based survey of nonelderly adults designed to assess how the COVID-19 pandemic is affecting adults and their families and how those effects change over time. A total of 4,007 adults ages 18 to 64 participated in the second wave, which was fielded September 11 through 28, 2020; 91 percent of respondents completed the survey between September 11 and 17. The first wave of the tracking survey was fielded May 14 through 27. Respondents for both waves were sampled from the 9,032 adults who participated in the most recent round of the Health Reform Monitoring Survey (HRMS), which was fielded March 25 through April 10, 2020. The HRMS sample is drawn from Ipsos's KnowledgePanel, the nation's largest probability-based online panel. The panel is recruited from an address-based sampling frame covering 97 percent of US households and includes households with and without internet access. Participants can take the survey in English or Spanish.

The Coronavirus Tracking Survey includes an oversample of Black and Hispanic/Latinx HRMS participants. Survey weights adjust for unequal selection probabilities and are poststratified to the characteristics of the national nonelderly adult population based on benchmarks from the Current Population Survey and American Community Survey. We also adjust the September tracking survey weights to address differential nonresponse among participants in the March/April HRMS. Because nonresponse in the September survey is greater among HRMS participants experiencing negative employment effects and material hardship during the pandemic and these effects differ based on demographic characteristics, we adjust the weights so work status and employment and hardship outcomes reported in March/April among the September sample are consistent with the outcomes reported among the full March/April HRMS sample both overall and within key demographic subgroups. These adjustments make the September tracking survey sample more representative of the sample initially drawn in March/April and mitigate nonresponse bias in estimated changes over time in the pandemic's effects.

The margin of sampling error, including the design effect, for the full sample of adults in the second wave of the tracking survey is plus or minus 2.0 percentage points for a 50 percent statistic at the 95 percent confidence level. Additional information about the March/April 2020 HRMS and the questionnaires for the HRMS and first and second waves of the Coronavirus Tracking Survey can be found at hrms.urban.org.

Analytic Approach

We asked survey respondents two questions about whether they did not get care because of the pandemic. The first asked whether there was ever a time when respondents needed several types of health care but did not get them because they were worried about being exposed to the coronavirus. The second question asked whether there was ever a time when respondents needed several types of health care but did not get them because a health care provider limited services because of the pandemic. Each question asked about the following types of care: prescription drugs; a general doctor

or specialist visit; going to a hospital; preventive health screenings or medical tests; treatment or follow-up care; dental care; mental health care or counseling; treatment or counseling for alcohol or drug use; or some other type of medical care. Those who reported not getting one or more types of care were asked whether they eventually got care (delayed care) or had still not gotten it at the time of the survey (forgone care).

We assessed differences in delayed and forgone care based on whether respondents were ever told by a doctor or other health professional that they had any of several chronic health conditions. We asked about conditions commonly included in federal health surveys and conditions the Centers for Disease Control and Prevention has identified as increasing a person's risk of moderate or severe illness from contracting COVID-19.[11] We also asked about height and weight to construct a measure of body mass index to define obesity.

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9 See the list of surveys in note 1 above.

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CORONAVIRUS BY THE NUMBERS

The Delta Variant Isn't As Contagious As Chickenpox. But It's Still Highly Contagious

August 11, 2021 · 5:28 AM ET
Heard on Morning Edition

MICHAELEEN DOUCLEFF

3-Minute Listen

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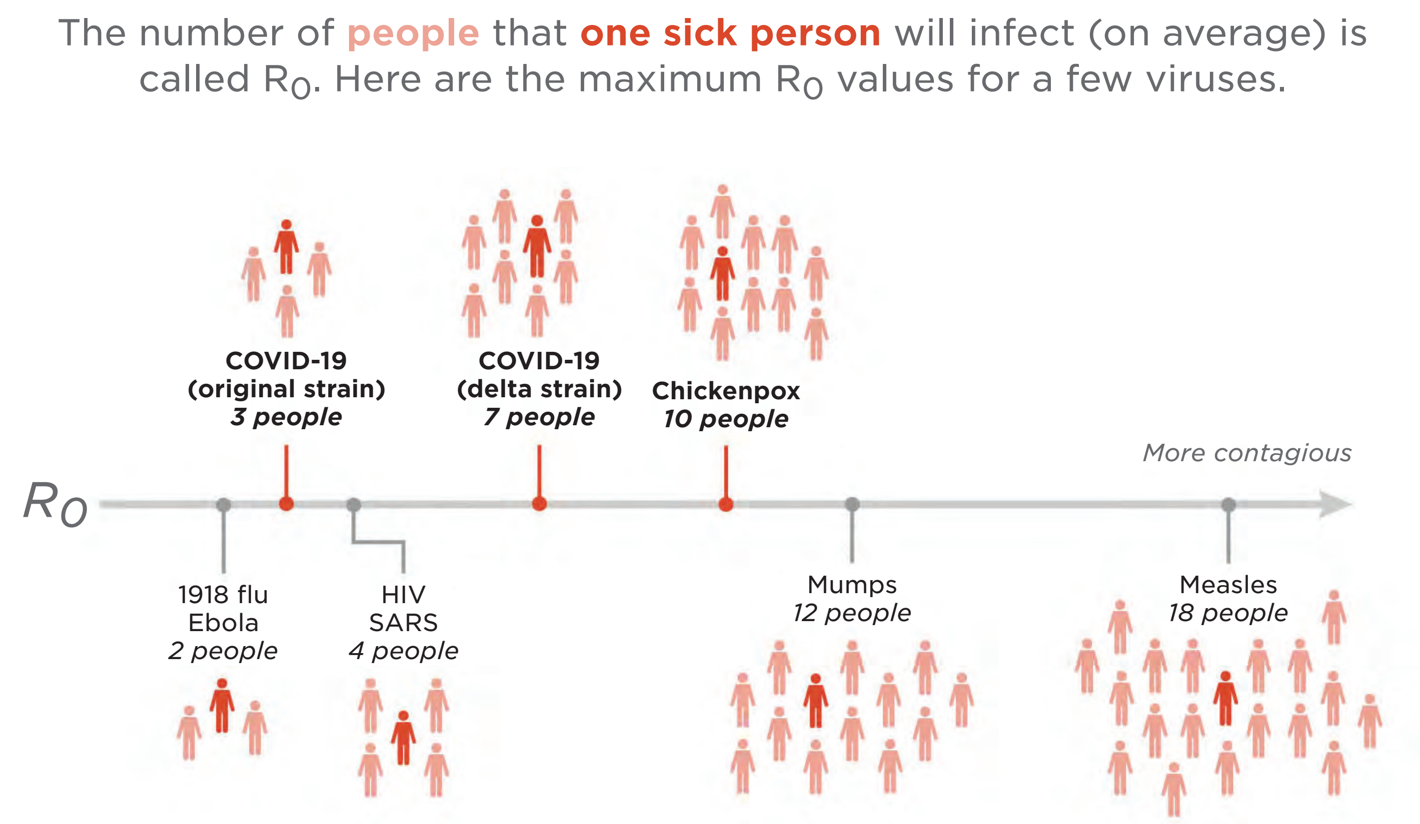
Transcript

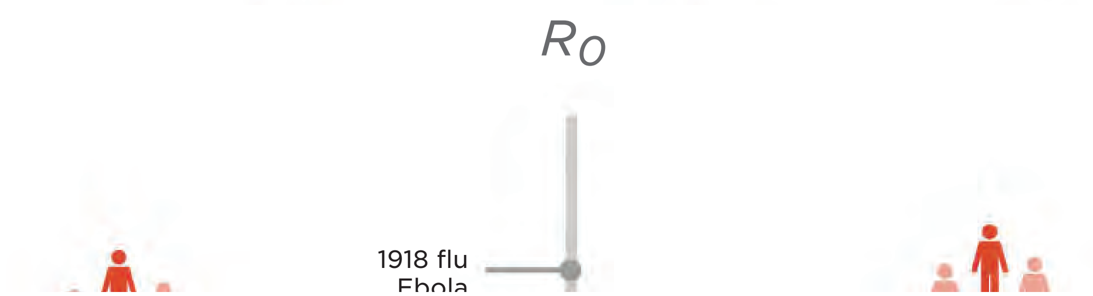
In a leaked report, the Centers for Disease Control and Prevention made a surprising claim about the delta variant of the coronavirus: It "is as transmissible as: - Chicken Pox," the agency wrote in a slideshow presentation leaked to *The Washington Post* on July 26.

Chickenpox is one of the most contagious viruses known. Each individual can spread the virus to as many as "90% of the people close to that person," the CDC reports.

Is the delta variant that contagious as well?

The short answer is no, says evolutionary biologist and biostatistician Tom Wenseleers at the University of Leuven in Belgium.





"Yeah, I didn't find the CDC's statement entirely accurate," says Wenseleers, who was one of the first scientists to formally calculate the transmission advantage of the alpha and delta variants over the original versions of SARS-CoV-2.

Nonetheless, delta is still highly transmissible, he adds. It's one of the most contagious respiratory viruses that we know of, he says.

Here's why.

When scientists measure a virus's transmissibility, they often use what's known as R0, or "R nought. " It's the number of people a sick person will infect when the entire population is vulnerable to the virus.

"So it's the virus's potential of spreading, given ideal conditions for the virus, when no one has any immunity," says computational biologist Karthik Gangavarapu at the Scripps Research Institute.

For example, the flu has an R0 of about two. Each person infected with flu passes the virus on to two people on average. Some people will infect more than two people, and some will infect fewer. But over time, the average will be about two.

Chickenpox, on the other hand, is way more contagious, Gangavarapu says. Chickenpox has an R0 of about nine or 10. So each person with chickenpox infects about 10 other people on average. Outbreaks are explosive.

For SARS-CoV-2, the R0 has actually risen over the course of the pandemic as the virus evolved. When the coronavirus first emerged in 2019, SARS-CoV-2 was slightly

more contagious than flu, Gangavarapu says. "The initial COVID-19 strain had an R0 between two and three."

Then about a year later, the virus began to mutate quickly. The alpha variant emerged, likely in the U.K., and was more transmissible than the original strain. A few months later, the delta variant emerged, most likely in India. It was even more transmissible than alpha.

"For the delta variant, the R0 is now calculated at between six and seven," Wenseleers says. So it's two- to three-times as contagious as the original version of SARS-CoV-2 (R0 = 2 to 3) but less contagious than the chickenpox (R0 = 9 to 10).

So why did the CDC say the delta variant was "just as transmissible as" the chickenpox?

For one, the leaked document underestimated the R0 for chickenpox and overestimated the R0 for the delta variant. "The R0 values for delta were preliminary and calculated from data taken from a rather small sample size," a federal official told NPR. The value for the chickenpox (and other R0s in the slideshow) came from a graphic from *The New York Times*, which wasn't completely accurate.

"At the end of the day, this delta variant is much more transmissible than the alpha variant," the official added. "That's the message people need to take from this." The official requested anonymity because they were not authorized to speak to the media on this topic.

The difference between an R0 of three and six is massive. For example, with the original strain of SARS-CoV-2, one person would infect about three people, and each of those people would infect three more. So after only two rounds of transmission, cases would rise by nine (3 x 3 = 9). After three rounds, cases would rise by 27 (3 x 3 x 3 = 27). But with the delta variant, the first person would infect six others, who would each then infect six more people. So after two rounds of transmission, cases would already rise by 36 (6 x 6 = 36). After three rounds, cases would surge by 216 (6 x 6 x 6 = 216).

With an R0 of six, delta will be extremely difficult to slow down unless populations reach high levels of vaccination, Wenseleers says. And even then surges in cases will still occur, as is now happening in Iceland and parts of the U.S. The vaccine is less than 90% effective at stopping infections with delta, meaning at least 1 in 10 people could have breakthrough infections. And vaccinated people can still spread the virus. In addition, people who aren't vaccinated have a very high risk of infection, Wenseleers says. "Anyone that chooses not to get vaccinated will in all likelihood get infected by the delta variant over the coming months."

For example, in San Francisco, daily case levels are rapidly rising toward those seen last winter despite the fact that more than 70% of the population is vaccinated, per San Francisco Department of Public Health reports.

Although cases of delta are inevitable, hospitalizations aren't, Wenseleers points out. "As long as people would get vaccinated, then we will not get huge wave of hospitalizations." For example, the city of San Francisco has had 3,041 people hospitalized with COVID-19 since March 18, 2020. Only 16 of them were fully vaccinated.

Clarification

Aug. 13, 2021

In an earlier version of this story, evolutionary biologist and biostatistician Tom Wenseleers at the University of Leuven in Belgium stated that the delta variant of the coronavirus was "probably the most contagious respiratory virus that we know, for the moment." Wenseleers clarifies that he was referring to viruses that primarily affect the respiratory tract. Although the primary infection with measles occurs in other tissues besides the respiratory tract, measles can cause a runny nose and sneezing. Its R0 factor makes it more contagious than the delta variant.

r0 alpha variant delta variant contagious coronavirus

CDC Centers for Disease Control and Prevention

COVID-19

Delta Variant: What We Know About the Science

Updated Aug. 26, 2021 Print

On July 27, 2021, CDC released updated guidance on the need for urgently increasing COVID-19 vaccination coverage and a recommendation for everyone in areas of substantial or high transmission to wear a mask in public indoor places, even if they are fully vaccinated. CDC issued this new guidance due to several concerning developments and newly emerging data signals.

First, a significant increase in new cases reversed what had been a steady decline since January 2021. In the days leading up to our guidance update, CDC saw a rapid and alarming rise in the COVID-19 case and hospitalization rates around the country.

- In late June, the 7-day moving average of reported cases was around 12,000. On July 27, the 7-day moving average of cases reached over 60,000. This case rate looked more like the rate of cases we had seen before the vaccine was widely available.

Second, new data began to emerge that the Delta variant was more infectious and was leading to increased transmissibility when compared with other variants, even in some vaccinated individuals. This includes recently published data from CDC and our public health partners, unpublished surveillance data that will be publicly available in the coming weeks, information included in CDC's updated Science Brief on COVID-19 Vaccines and Vaccination, and ongoing outbreak investigations linked to the Delta variant.

Delta is currently the predominant variant of the virus in the United States. Below is a high-level summary of what CDC scientists have recently learned about the Delta variant. More information will be made available when more data are published or released in other formats.

Infections and Spread

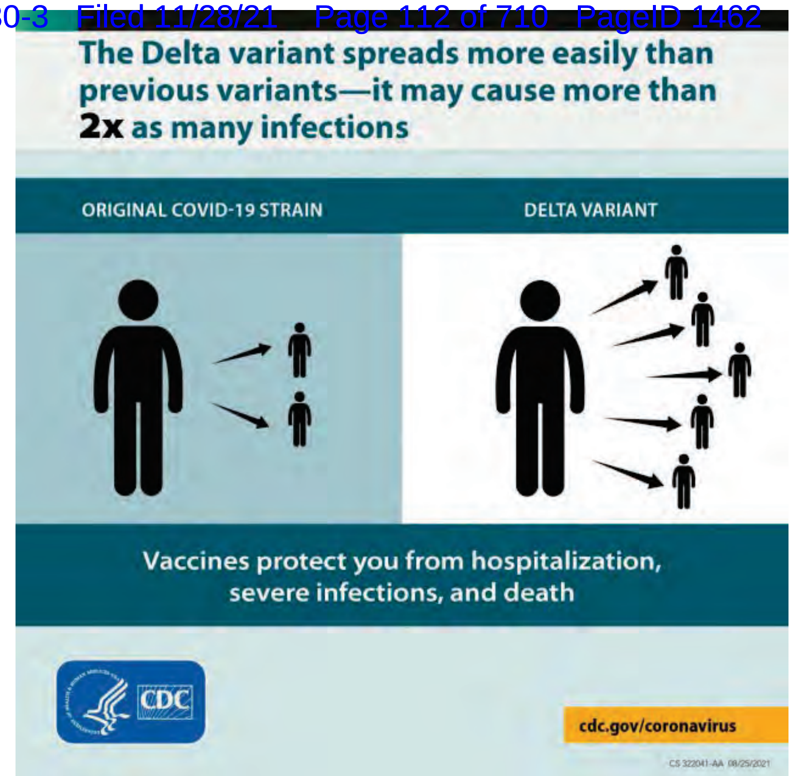
The Delta variant causes more infections and spreads faster than early forms of SARS-CoV-2, the virus that causes COVID-19

- **The Delta variant is more contagious:** The Delta variant is highly contagious, more than 2x as contagious as previous variants.
- **Some data suggest the Delta variant might cause more severe illness than previous variants in unvaccinated people**. In two different studies from Canada and Scotland, patients infected with the Delta variant were more likely to be hospitalized than patients infected with Alpha or the original virus that causes COVID-19. Even so, the vast majority of hospitalization and death caused by COVID-19 are in unvaccinated people.
- **Unvaccinated people remain the greatest concern:** The greatest risk of transmission is among unvaccinated people who are much more likely to get infected, and therefore transmit the virus. Fully vaccinated people get COVID-19 (known as breakthrough infections) less often than unvaccinated people. People infected with the Delta variant, including fully vaccinated people with symptomatic breakthrough infections, can transmit the virus to others. CDC is continuing to assess data on whether fully vaccinated people with asymptomatic breakthrough infections can transmit the virus.
- **Fully vaccinated people with Delta variant breakthrough infections can spread the virus to others. However, vaccinated people appear to spread the virus for a shorter time:** For prior variants, lower amounts of viral genetic material were found in samples taken from fully vaccinated people who had breakthrough infections than from unvaccinated people with COVID-19. For people infected with the Delta variant, similar amounts of viral genetic material have been found among both unvaccinated and fully vaccinated people. However, like prior variants, the amount of viral genetic material may go down faster in fully vaccinated people when compared to unvaccinated people. This means fully vaccinated people will likely spread the virus for less time than unvaccinated people.

Vaccines

Vaccines in the US are highly effective, including against the Delta variant

- The COVID-19 vaccines approved or authorized in the United States are highly effective at preventing severe disease and death, including against the Delta variant. But they are not 100% effective, and some fully vaccinated people will become infected (called a breakthrough infection) and experience illness. For all people, the vaccine provides the best protection against serious illness and death.



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- Vaccines are playing a crucial role in limiting spread of the virus and minimizing severe disease. Although vaccines are highly effective, they are not perfect, and there will be vaccine breakthrough infections. Millions of Americans are vaccinated, and that number is growing. This means that even though the risk of breakthrough infections is low, there will be thousands of fully vaccinated people who become infected and able to infect others, especially with the surging spread of the Delta variant. Low vaccination coverage in many communities is driving the current rapid surge in cases involving the Delta variant, which also increases the chances that even more concerning variants could emerge.
- Vaccination is the best way to protect yourself, your family, and your community. High vaccination coverage will reduce spread of the virus and help prevent new variants from emerging. CDC recommends that everyone aged 12 years and older get vaccinated as soon as possible.

Masks

Given what we know about the Delta variant, vaccine effectiveness, and current vaccine coverage, layered prevention strategies, including wearing masks, are needed to reduce the transmission of this variant

- At this time, as we build the level of vaccination nationwide, we must also use all the prevention strategies available, including masking indoors in public places, to stop transmission and stop the pandemic. Everyone who is able, including fully vaccinated people, should wear masks in public indoor places in areas of substantial or high transmission.

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Michigan Health Watch

Despite protests, 98% of Henry Ford Hospital workers get COVID vaccinations

Henry Ford Health System said it was losing about 400 workers who had refused to get a COVID vaccine, but was working rapidly to replace them. (James R. Martin / Shutterstock.com)

September 13, 2021

Robin Erb

Michigan Health Watch

Coronavirus Michigan

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Michigan Health Watch

Despite protests, 98% of Henry Ford Hospital workers get COVID vaccinations

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Oct. 5: **400 workers out, 1,900 exempt after Henry Ford COVID vaccine mandate**
Sept. 27: **Michigan hospitals eye nurses in other countries to fill COVID shortage**
Sept. 15: **ER's nearly full, Beaumont asks patients to go elsewhere if possible**

With the threat of job loss and a new federal mandate, nearly all of Henry Ford Health System's staff got vaccinated for COVID-19 or sought a religious or medical exemption.

In June, the Detroit-based system became the first hospital in Michigan to mandate vaccines among its staff, students, volunteers and contractors.

Despite protests and the threat of litigation, 98 percent of the system's 33,000 workers were fully or partially vaccinated or in the process of obtaining a religious or medical exemption when the requirement went into effect Friday, Henry Ford officials said Monday.

Related:

- A Michigan doctor goes to Facebook over dying, unvaccinated COVID patients
- Michigan COVID nurses reach their limit: 'I know I can't do this forever'
- Michigan labs fear COVID test shortages. Will new mandates add to strain?
- Required COVID vaccines put Michigan hospital worker hesitancy to the test

Exemptions comprise less than 1 percent of staffers, while the remaining workers who haven't been vaccinated face a three-week unpaid suspension if they continue to refuse.

"Those team members will then have until Friday, Oct. 1, to change their mind," Bob Riney, Henry Ford's president of healthcare operations and chief operating officer, said Monday during a media conference.

"If they receive the first dose before Oct. 1, they can immediately return to work. Should a team member choose not to get vaccinated by Oct. 1, they will voluntarily resign from our organization."

Employees who refuse vaccinations and "voluntarily resign," would be allowed to reapply for their jobs once they are vaccinated, Riney said. Those who refuse to be vaccinated or voluntarily resign will be fired, he said.

Precise numbers of refusers weren't available Monday, but the low numbers appear to show that while vaccine mandates remain divisive with the public, most workers eventually get the shots to keep their jobs.

Another system, Houston Methodist Hospital in Texas, had only 153 of 25,000 employees quit or be fired when it became the first hospital network in the nation to require inoculations as a condition of employment in April.

(In general, legal experts say those who are fired for refusing vaccines cannot qualify for unemployment benefits because they violated company policy.)

Henry Ford's announcement follows President Joe Biden's decision Thursday to require all workplaces with more than 100 employees to mandate vaccinations or weekly testing.

The rule, which also covers all hospital workers, would impact 100 million workers nationwide and more than 2 million in Michigan.

Even before Biden's announcement, most — but not all — large hospital systems in Michigan had followed Henry Ford's lead and required vaccines. That's been a gambit for providers, who are struggling to attract and keep workers amid a pandemic.

The shortages forced Henry Ford to close 120 general medicine and intensive care beds, Dr. Adnan Munkarah, the system's executive vice president and chief clinical officer said Monday.

He said the closures have not affected patient care because they are spread throughout the system, which has five hospitals and 2,000 beds.

Riney said vaccine rates have increased because of Biden's mandate and the U.S. Food and Drug Administration's decision in August to give full approval to the Pfizer vaccine, eliminating the worry among some that they were being asked to be vaccinated with an unlicensed vaccine.

"We believe that that tipped the scales for some team members who are on the fence," Riney said.

Henry Ford's decision had prompted protests from hundreds of workers, but a day after the Biden announcement, staffers dropped their lawsuit challenging the health system's mandate. They had argued that the mandate violated their constitutional rights.

"Whatever has driven their change of heart, we are encouraged to see so many following the science," Riney said, speaking generally about those who recently decided to be vaccinated.

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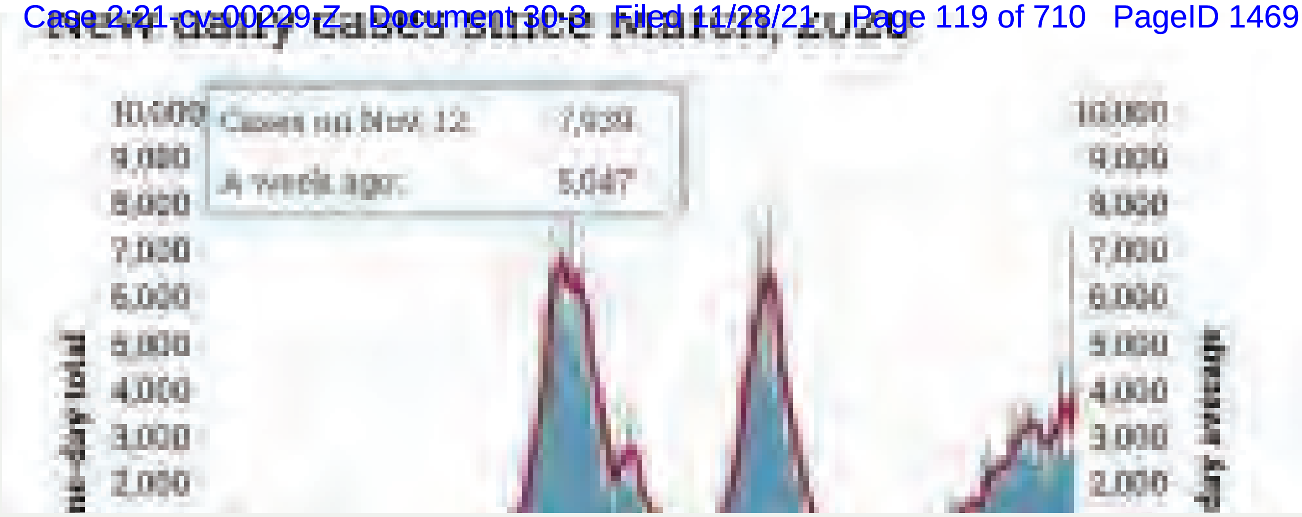

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COVID-19

Developing COVID-19 Vaccines

Updated Sept. 8, 2021 Print

Overview

Bringing a new vaccine to the public involves many steps including vaccine development, clinical trials, U.S. Food and Drug Administration (FDA) authorization or approval, manufacturing, and distribution. Many different public organizations and private companies have worked together to make COVID-19 vaccines available to the public. While COVID-19 vaccines were developed rapidly, all steps have been taken to ensure their safety and effectiveness.

The Vaccine Process: From the Lab to You

Initial Development

New vaccines are first developed in laboratories. Scientists have been working for many years to develop vaccines against coronaviruses, such as those that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). SARS-CoV-2, the virus that causes COVID-19, is related to these other coronaviruses. The knowledge that was gained through past research on coronavirus vaccines helped speed up the initial development of the current COVID-19 vaccines.

Clinical Trials

After initial development, vaccines go through three phases of clinical trials to make sure they are safe and effective. For other vaccines routinely used in the United States, the three phases of clinical trials are performed one at a time. During the development of COVID-19 vaccines, these phases overlapped to speed up the process so the vaccines could be used as quickly as possible to control the pandemic. No trial phases have been skipped.

The clinical trials for COVID-19 vaccines have involved tens of thousands of volunteers of different ages, races, and ethnicities. Clinical trials for vaccines compare outcomes (such as how many people get sick) between people who are vaccinated and people who are not. Because COVID-19 continues to be widespread, the vaccine clinical trials have been conducted more quickly than if the disease were less common. Results from these trials have shown that COVID-19 vaccines are effective, especially against severe illness, hospitalization, and death.

The clinical trials showed no serious safety concerns within 8 weeks following vaccination. This is an important milestone, as it is unusual for adverse effects caused by vaccines to appear after this amount of time. Now that COVID-19 vaccines are available to the public, CDC and FDA continue to monitor their safety and alert the public about health problems that are reported after vaccination.

Authorization or Approval

Before vaccines are made available to people in real-world settings, FDA assesses the findings from clinical trials. Initially, they determined that three COVID-19 vaccines met FDA's safety and effectiveness standards and granted those vaccines Emergency Use Authorizations (EUAs). The EUAs allowed the vaccines to be quickly distributed for use while maintaining the same high safety standards required for all vaccines. Learn more in this video about EUAs.

FDA has now granted full approval for Pfizer-BioNTech (COMIRNATY) COVID-19 Vaccine for people age 16 years and older. Before granting approval, FDA reviewed evidence that built on the data and information submitted to support the EUA. This included preclinical and clinical trial data and information, as well as details of the manufacturing process, vaccine testing results to ensure vaccine quality, and inspections of the sites where the vaccine is made. This vaccine was found to meet the high standards for safety, effectiveness, and manufacturing quality FDA requires of an approved product. Learn more about the process for FDA approval.

Manufacturing and Distribution

The U.S. government has invested substantial resources for both manufacturing and distribution of COVID-19 vaccines. This allowed manufacturing to begin when the vaccines were still in the third phase of clinical trials so that distribution could begin as soon as FDA authorized each vaccine.

Tracking Safety Using Vaccine Monitoring Systems

As vaccines are distributed outside of clinical trials, several monitoring systems continue to track them to ensure their safety. Hundreds of millions of people in the United States have received COVID-19 vaccines under the most intense safety monitoring in U.S. history. Some people have no side effects. Many people have reported common side effects after COVID-19 vaccination, like pain or swelling at the injection site, a headache, chills, or fever. These reactions are common and are normal signs that your body is building protection.

Reports of serious adverse events after vaccination are rare. CDC and FDA continue to closely monitor several reporting systems, like the Vaccine Adverse Event Reporting System (VAERS), Vaccine Safety Datalink (VSD), and v-safe, which help look for safety issues now that the vaccines are being given to patients in real-world settings across the country. CDC provides timely updates on selected serious adverse events reported after COVID-19 vaccination.

What This Means for You

COVID-19 vaccines have been rapidly developed and distributed to help fight the pandemic. During this process, all steps have been taken to ensure their safety and effectiveness. CDC recommends you get a COVID-19 vaccine as soon as you can to help protect yourself and others.

Related Pages

- Different COVID-19 Vaccines
- Possible Side Effects After Getting a COVID-19 Vaccine
- What to Do if You Had an Allergic Reaction After Getting a COVID-19 Vaccine
- V-safe after Vaccination Health Checker
- Understanding mRNA COVID-19 Vaccines

For Healthcare Professionals

- Quick Answers for Healthcare Professionals [217 KB, 2 Pages]
- Answering Your Questions About the New COVID-19 Vaccines [368 KB, 4 Pages]
- COVID-19 Vaccine Basics: What Healthcare Personnel Need to Know [1.32 MB, 23 Pages]
- COVID-19 Vaccination Communication Toolkit
- COVID-19 Vaccination: Clinical Resources for Each COVID-19 Vaccine

More Information

COVID-19, MERS & SARS

Vaccine Development Process: How Was Time Saved [779 KB, 1 Page]

FDA Approves First COVID-19 Vaccine

Last Updated Sept. 8, 2021

CDC Centers for Disease Control and Prevention

Dialysis COVID-19 Vaccination Data Dashboard

Overview

Dialysis facilities report COVID-19 data to CDC's National Healthcare Safety Network (NHSN), including weekly vaccination data for patients and weekly vaccination data for healthcare personnel (HCP).

CDC began collecting weekly vaccination data, reported voluntarily through the Dialysis COVID-19 Module on March 11, 2021. The Centers for Medicare and Medicaid Services' (CMS) End Stage Renal Disease (ESRD) Network program established COVID-19 vaccination reporting requirements beginning March 17, 2021.

This page displays data at the national and state level on COVID-19 vaccination coverage among patients and staff of dialysis facilities. These summaries represent data that dialysis facilities reported to the NHSN Dialysis COVID-19 Module using weekly vaccination forms.

CDC updates this data dashboard weekly on Thursday at 8 a.m. Eastern. As a result, the figures presented on this page may not exactly match data publicly posted by state health departments or other federally coordinated programs.

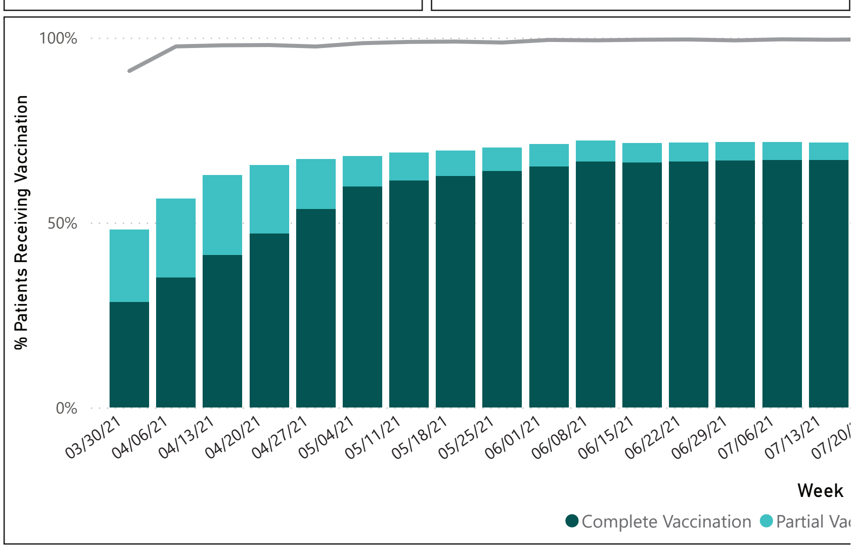
IMPORTANT: Data displayed on this page were submitted directly to CDC's National Healthcare Safety Network (NHSN) and do not include data submitted to other entities contracted by or within the local, state, or federal government.

COVID-19 Vaccination Coverage and Reporting among Patients in Dialysis Facilities, by Week - United States

COVID-19 Vaccination Coverage amon
week—Unite

Select By State: All

Select By Region: All



All data can be modified from week-to-week by facili es. Exclusions: for best epidemiological understandin
Vaccina on coverage is calculated as the total number of pa ents vaccinated divided by (the total number
or exclusions to vaccina on) mul plied by 100. Differences in how each facility implements this COVID-19

COVID-19 Vaccination Coverage and Reporting among Patients in Dialysis Facilities, by State and Week - United States

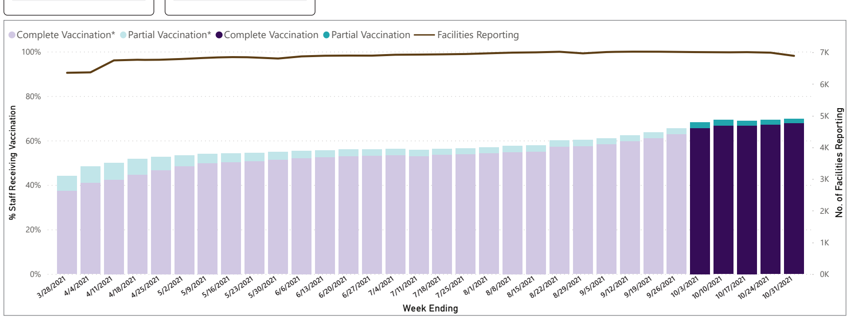
COVID-19 Vaccination Coverage and Reporting among Staff in Dialysis Facilities, by Week - United States

COVID-19 Vaccination Coverage and Reporting among Staff in Dialysis Facilities, by week—United States

Partial vaccination: 1 dose of a 2 dose mRNA vaccination series. **Complete vaccination**: All doses required to be fully vaccinated (two doses of a two-dose mRNA series or one dose of a single-dose vaccine).

Select By State: All

Select By Region: All



All data can be modified from week-to-week by facili es. Exclusions: for best epidemiological understanding, data that appear inconsistent with surveillance protocols are excluded. Vaccina on coverage is calculated as the total number of staff vaccinated divided by (the total number of staff minus the number of staff with medical contraindica ons or exclusions to vaccina on) mul plied by 100. Differences in how each facility implements this COVID-19 vaccina on data collec on, including varia on in which staff collect the data, may affect facility repor ng pa erns.

*As of week-ending 10/3/2021, the staff categories that make up the denominator for staff vaccina on coverage were modified to match those used for repor ng influenza vaccina on coverage.

Data source: Centers for Disease Control and Preven on, Na onal Healthcare Safety Network **Accessibility**: [Right click on the graph area to show as table]

COVID-19 Vaccination Coverage and Reporting among Staff in Dialysis Facilities, by State and Week - United States

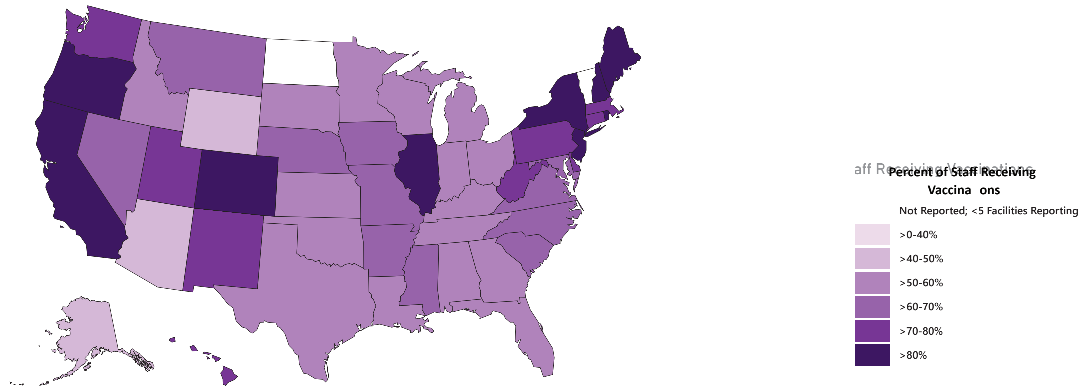
COVID-19 Vaccination Coverage among Staff in Dialysis Facilities, by State—United States

Data as of 11/8/2021
5:30 AM

Select By Coverage: Complete

Select By Week: Most Recent Week

Percentage of Staff Receiving Complete Vaccinations during the Week of 10/25/2021 - 10/31/2021



All data can be modified from week-to-week by facili es. Exclusions: for best epidemiological understanding, data that appear inconsistent with surveillance protocols are excluded. Vaccina on coverage is calculated as the total number of staff vaccinated divided by (the total number of staff minus the number of staff with medical contraindica ons or exclusions to vaccina on) mul plied by 100. Differences in how each facility implements this COVID-19 vaccina on data collec on, including varia on in which staff collect the data, may affect facility repor ng pa erns.

Defini ons: **Par al vaccina on:** 1 dose of a 2 dose mRNA vaccina on series. **Complete vaccina on**: All doses required to be fully vaccinated (two doses of a two-dose mRNA series or one dose of a single-dose vaccine).

Data source: Centers for Disease Control and Preven on, Na onal Healthcare Safety Network

For more informa on: h ps://www.cdc.gov/nhsn/dialysis/covid19/index.html

Accessibility: [Right click on the graph area to show as table]

Microsoft Power BI

Page last reviewed: August 12, 2021

CDC Centers for Disease Control and Prevention

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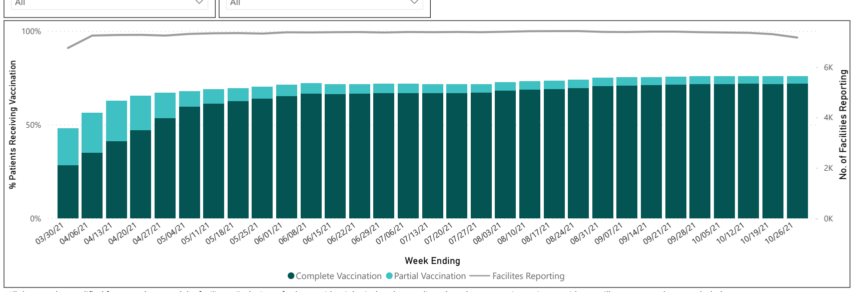
COVID-19 Vaccination Coverage and Reporting among Patients in Dialysis Facilities, by Week - United States

COVID-19 Vaccination Coverage among Patients in Dialysis Facilities, by week—United States

Data as of 11/1/2021 5:30 AM

Select By State: All

Select By Region: All



All data can be modified from week-to-week by facili es. Exclusions: for best epidemiological understanding, data that appear inconsistent with surveillance protocols are excluded. Vaccina on coverage is calculated as the total number of pa ents vaccinated divided by (the total number of pa ents minus the number of pa ents with medical contraindica ons or exclusions to vaccina on) mul plied by 100. Differences in how each facility implements this COVID-19 vaccina on data collec on, including varia on in which staff collect the data, may affect facility repor ng pa erns.

Defini ons: Par al vaccina on: 1 dose of a 2 dose mRNA vaccina on series. **Complete vaccina on:** All doses required to be fully vaccinated (two doses of a two-dose mRNA series or one dose of a single-dose vaccine).

Data source: Centers for Disease Control and Preven on, Na onal Healthcare Safety Network

For more informa on: h ps://www.cdc.gov/nhsn/dialysis/covid19/index.html

Accessibility: [Right click on the graph area to show as table]

COVID-19 Vaccination Coverage and Reporting among Patients in Dialysis Facilities, by State and Week - United States

Microsoft Power BI

COVID-19 Vaccination Coverage and Reporting among Staff in Dialysis Facilities, by Week - United States

Microsoft Power BI

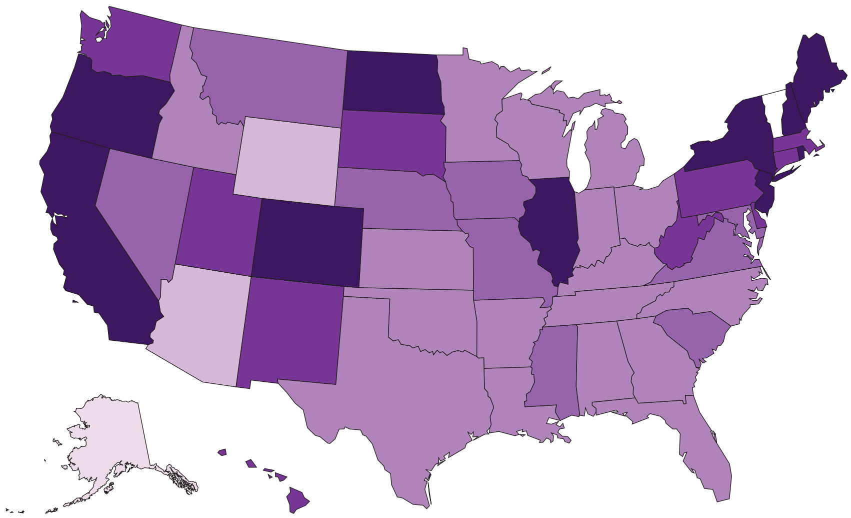
COVID-19 Vaccination Coverage and Reporting among Staff in Dialysis Facilities, by State and Week - United States

COVID-19 Vaccination Coverage among Staff in Dialysis Facilities, by State—United S

Select By Coverage
Complete

Select By Week
Most Recent Week

Percentage of Staff Receiving Complete Vaccinations during the Week of 10/18/2021 - 10/24



All data can be modified from week-to-week by facili es. Exclusions: for best epidemiological understanding, data that appear inconsistent with surveillance protocols are excl

Microsoft Power BI

Page last reviewed: August 12, 2021

Centers for Disease Control and Prevention

COVID-19

Different COVID-19 Vaccines

Updated Sept. 1, 2021 Print

Cases of myocarditis and pericarditis in adolescents and young adults have been reported more often after getting the second dose than after the first dose of one of the two mRNA COVID-19 vaccines, Pfizer-BioNTech or Moderna. **These reports are rare and the known and potential benefits of COVID-19 vaccination outweigh the known and potential risks, including the possible risk of myocarditis or pericarditis.**

Authorized and Recommended Vaccines

Currently, three vaccines are authorized and recommended in the United States to prevent COVID-19:

Pfizer-BioNTech

Moderna

Johnson & Johnson / Janssen

Different COVID-19 Vaccines

Vaccines are now widely available. In most cases, you do need an appointment. Do not wait for a specific brand. Learn how to find a COVID-19 vaccine so you can get it as soon as you can.

All currently authorized and recommended COVID-19 vaccines:

- are safe,
- are effective, and
- reduce your risk of severe illness.

CDC does not recommend one vaccine over another.

People with moderately to severely compromised immune systems should receive an additional dose of mRNA COVID-19 vaccine after the initial 2 doses.

Learn more about Booster Shots.

Vaccine Brand Name	Who Can Get this	How Many Shots You	When Are You Fully

Vaccine Brand Name	Vaccine [1]	Will Need	Vaccinated?
Pfizer-BioNTech	People 12 years and older	**2 shots** Given 3 weeks (21 days) apart [2]	2 weeks after your second shot
Moderna	People 18 years and older	**2 shots** Given 4 weeks (28 days) apart [2]	2 weeks after your second shot
Johnson & Johnson's Janssen	People 18 years and older	**1 shot**	2 weeks after your shot

[1] If you have had a severe allergic reaction (anaphylaxis) or an immediate allergic reaction to any ingredient in the vaccine you are scheduled to receive, you should not get that vaccine. If you have been instructed not to get one type of COVID-19 vaccine, you may still be able to get another type. Learn more information for people with allergies.

[2] You should get your second shot as close to the recommended 3-week or 4-week interval as possible. However, your second shot may be given up to 6 weeks (42 days) after the first dose, if necessary.

Vaccine Types

Understanding How COVID-19 Vaccines Work
Learn how the body fights infection and how COVID-19 vaccines protect people by producing immunity. Also see the different types of COVID-19 vaccines that currently are available or are undergoing large-scale (Phase 3) clinical trials in the United States.

COVID-19 mRNA Vaccines
Information about mRNA vaccines generally and COVID-19 vaccines that use this new technology specifically.

Viral Vector COVID-19 Vaccines
Information about viral vector vaccines generally and COVID-19 vaccines that use this new technology specifically.

Vaccines in Phase 3 Clinical Trials

Large-scale (Phase 3) clinical trials are in progress or being planned for COVID-19 vaccines in the United States. To learn more about U.S. COVID-19 vaccine clinical trials, including vaccines in earlier stages of development, by visiting clinicaltrials.gov.

For Healthcare Professionals

COVID-19 Clinical Resources

Last Updated Sept. 1, 2021

Direct Care Worker Retention:
Strategies for Success

Commissioned by the AAHSA Talent Cabinet January 2010

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Direct Care Worker Retention: Strategies for Success

Author: Linda Barbarotta, Institute for the Future of Aging Services, AAHSA

AAHSA Talent Cabinet

The American Association of Homes and Services for the Aging (AAHSA) established the AAHSA Talent Cabinet in 2007 to develop recommendations for policy, practice and education changes that address the current and projected long-term care workforce shortages.

The Cabinet's objectives:

- Review the most current research on what it takes to recruit and retain a well-trained and quality workforce across the long-term care continuum of services, with the focus on administrators, nurses (registered nurses, licensed practical nurses), direct care workers (certified nursing assistants, home health aides), medical directors, social workers and pharmacists.
- Gather and synthesize special initiatives and "best practices" identified by stakeholders for the benefit of members and other aging services providers
- Provide recommendations for policy, practice and education changes to achieve this goal
- Propose strategies needed to implement these recommendations

The Cabinet is comprised of AAHSA members, other aging service providers, direct care workers, consumers and representatives from education, research, workforce development, state government and state boards of nursing.

AAHSA

The members of the American Association of Homes and Services for the Aging (www.aahsa.org) help millions of individuals and their families every day through mission-driven, not-for-profit organizations dedicated to providing the services that people need, when they need them, in the place they call home. Our 5,700 member organizations, many of which have served their communities for generations, offer the continuum of aging services: adult day services, home health, community services, senior housing, assisted living residences, continuing care retirement communities and nursing homes. AAHSA's commitment is to create the future of aging services through quality people can trust.

Institute for the Future of Aging Services

The Institute for the Future of Aging Services (IFAS) is a policy research institute whose mission is to create a bridge between the practice, policy and research communities to advance the development of high-quality health, housing and supportive services for America's aging population. IFAS is the applied research arm of the American Association of Homes and Services for the Aging (AAHSA).

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Table of Contents

I.

Introduction and Background

This report, commissioned by the American Association of Homes and Services for the Aging (AAHSA) Talent Cabinet, documents the research and programs shown to increase the retention of direct care workers in long-term care. Aging-services providers and other long-term care stakeholders can use this report to learn more about the factors that lead to increased retention and about the various retention strategies and programs currently in place.[1]

The Role of Direct Care Staff

Direct care workers—nursing assistants or nurse aides, home health aides, home care aides and personal care workers and personal service attendants—form the centerpiece of the formal long-term care system (**Stone and Weiner 2001; DHHS 2006; Stone and Dawson 2008**). These frontline caregivers provide hands-on care to millions of elderly and younger people with disabilities in nursing homes and assisted living residences, in community settings and in private homes. Direct care workers provide eight out of every 10 hours of paid care received by a long-term care consumer. They often are referred to as the "eyes and the ears" of the care system (**Stone and Dawson 2008**). In addition to helping with daily-living activities (e.g., bathing, dressing, using the toilet and eating), these workers provide the "high touch" that is essential to quality of life, as well as quality of care, for elders and chronically disabled individuals.

How Many Direct Care Workers Will Be Needed?

According to the U.S. Bureau of Labor Statistics (BLS), in 2006 there were an estimated 1.4 million nurse aides, orderlies and attendants, largely employed in nursing homes. Another 787,000 home health aides provided care mostly in home-based care settings, and 767,000 worked as personal and home care aides, with two-thirds of those employed in home-based services (**BLS, Occupational Outlook Handbook 2009**).

[1] A second report, *Retention Strategies for the Professional Long-Term Care Staff*, examines the research and programs pertaining to the retention of professional long-term care staff: long-term care administrators, medical directors, nurses, pharmacists and social workers.

Because the U.S. population is aging and persons with disabilities are living longer, the demand for these workers will increase sharply. In fact, personal and home care aides, and home health aides are the second and third fastest-growing occupations in the United States (**BLS, Occupational Outlook Handbook 2009**). All three occupations—nursing assistant or nurse aide, home health aide, and personal and home care aide—are among the 30 occupations projected to have the largest employment growth.

BLS estimates the number of home health aides will grow by 49 percent between 2006 and 2016. This means by 2016, 384,000 more home health aides will be needed. The number of personal and home care aides is expected to grow by 51 percent, with 389,000 needed to fill these positions. The growth in nurse aides, orderlies and attendants is projected to increase 18 percent, with 264,000 more needed by 2016 (**Dohm and Sniper 2007**).

Challenges of High Turnover

Added to the growing demand for direct care staff is a challenge facing many long-term care providers today—the high turnover rates of direct care staff. In the sixth national survey of state initiatives and public policy actions on the direct care workforce, 97 percent of the Medicaid agencies and state units on aging completing the survey considered direct care vacancies and turnover a serious workforce issue (**Dyson and Harmuth 2007**).

According to a 2007 American Health Care Association (AHCA) survey, the turnover rate for certified nursing assistants in nursing homes was 65.6 percent (**AHCA 2008**). For home health aides, one study estimated that the turnover rate of home health aides who had been on the job for less than a year was 40 to 60 percent, with 80 to 90 percent leaving within the first year (**PHI and IFAS 2005**). Staff turnover in assisted living residences ranges from 21 to 135 percent, averaging 42 percent (**Maas and Buckwalter 2006**).

The reasons for this high turnover rate are varied. Although the jobs themselves are rewarding for many direct care workers, workers often face such challenges as low pay, a lack of health insurance, poor or inadequate training, little or no advancement opportunities, poor relationships with their supervisors, physical and emotional demands, and lack of respect by management, residents' families and society.

Even though providers are reporting lower staff turnover during this current economic downturn and tight labor market, providers also have seen turnover increase during times of stronger economic growth. In addition, projections show the field will experience an overall shortage of people available to enter the pipeline and fill future direct care worker positions. Because of the instability of relying on economic cycles and the upcoming shortfall of potential workers, the underlying problems associated with direct care jobs must be addressed in order to ensure a stable, committed workforce. High turnover rates impact the quality of care provided to residents and clients, and the financial health of aging-services providers.

According to Castle and associates, high turnover rates of certified nursing assistants, licensed practical nurses and registered nurses, in general, are associated with worse quality of care for nursing home residents (**Castle, Engberg and Men 2007**). In the study, the authors examined the association between staff turnover and quality, using 14 indicators of care quality found in Nursing Home Compare. These indicators include rates of moderate to severe pain, pressure sores, physical restraint

use, catheter use, mobility, loss of bladder or bowel control, and increased depression or anxiety. The analysis showed that an increase in turnover from medium (40-80 percent per year) to high levels (more than 80 percent per year) was associated with lower quality factor scores, although even higher levels of turnover were not associated with a further decrease in quality.

In an earlier study, Castle and Engberg found higher quality of care was associated with lower nursing staff turnover in 854 nursing homes in six states (**Castle and Engberg 2006**).

Bostick and colleagues conducted a systematic review of 87 research articles and government documents published from 1975 to 2003 to determine the link between staffing and quality measures in nursing homes. The researchers found a significant relationship between high staff turnover and poor quality outcomes for residents (**Bostick et al. 2006**). Higher turnover rates in nursing homes have been associated with greater use of physical restraints, catheters and psychoactive drugs, as well as more contractures, pressure ulcers and quality-of-care deficiencies (**Harahan and Stone 2009, 233-53**).

High turnover rates also affect providers' financial health. Many providers are unaware how much direct care worker turnover actually costs. An estimate of the minimum direct cost of replacing a direct care worker is $2,500. This does not take into account the indirect costs of turnover: lost productivity until a replacement is trained, lost client revenues and/or reimbursement, increases in worker injuries, clients' physical and emotional stress, and a deterioration of working conditions possibly leading to more turnover (**Seavey 2005**). The estimate of the direct and indirect average turnover cost is significant: $3,500 per direct care worker.

Direct care worker turnover impacts long-term care providers on many levels, and they would benefit from strategies that improve retention.

II.

How the Report Is Organized

This report is organized into two main sections. **Section III** includes key research findings in the professional literature that show which factors lead to an increase in direct care worker retention. **Section IV** describes key retention strategies and programs shown to have a positive impact on direct care worker retention.

Both **Sections III** and **IV** cover the following areas:

- Competitive wages and health insurance benefits
- Culture change
- Workplace/job design, management practices and trained supervisors
- Comprehensive training
- Career advancement opportunities
- Importance of cultural competence

Section V includes additional tools and resources related to direct care worker retention. **Section VI** is the list of references.

III.

Research: What It Takes to Increase Direct Care Worker Retention

This section presents the research studies and evidence that show which factors support higher direct care worker retention. The factors we cover in this section include:

A. **Competitive wages and health insurance benefits**

B. **Overarching strategy of culture change**

C. **Overarching strategies of workplace/ job design, management practices and trained supervisors**

D. **Comprehensive training needed to deliver quality care**

E. **Career advancement opportunities (peer mentoring, career ladders)**

F. **The importance of cultural competence**

The Institute of Medicine (IOM) report, Retooling for an Aging America: Building the Health Care Workforce, focused on similar factors contributing to direct care worker retention: improving training, increasing financial incentives, and improving the work environment through empowerment strategies and culture change (**IOM 2008**).

A. Competitive Wages and Health Insurance Benefits

Direct care workers receive some of the lowest wages in the United States. According to PHI, the median hourly wage in 2007 for all direct care workers was $10.48, significantly less than the median wage of $15.10 for all U.S. workers (**PHI 2009**). About 45 percent of direct care workers are in households under 200 percent of the poverty line, making them eligible for state and federal public assistance programs. Two out of five direct care workers receive one or more public benefits (**PHI 2009**).

Health insurance coverage for direct care workers is just as dismal. One in every four nursing home workers and nearly one third of personal and home care aides lack health coverage, and only 53 percent have coverage from their employer (**PHI 2009**).

Impact of Wages and Health Insurance on Probability of Becoming a Direct Care Worker: Rodin looked at the effect of wage increases and the availability of health insurance on the probability of workers becoming certified nursing assistants (CNAs). He found that making health insurance available to workers had a large positive impact on the probability they would choose to become CNAs. However, the combination of increased wages and health insurance would result in the largest net gain in the number of CNAs (**Rodin 2005**).

Studies of Job Tenure (Length of Time on Job): A study based on data from the 2004 National Nursing Home Survey, the National Nursing Assistant Survey and the Area Resource File looked at whether wages, benefits, training and organizational culture had an effect on increasing the job tenure of CNAs in nursing homes. Overall, it was the extrinsic rewards of higher wages, benefits such as paid time off and a pension that were the most important determinants of job tenure (**Weiner et al. 2009**).

Frontline health care workers enrolled in employer health insurance plans have more than twice the tenure of those without employee coverage (**Duffy 2004, as cited in PHI 2008, The Invisible Care Gap**).

Better Wages and Health Insurance Can Help Increase Retention: In several studies, higher wages and access to health insurance have shown a significant impact on the retention of direct care workers.

Using data from the 2004 National Nursing Assistant Survey, Decker and colleagues showed that satisfaction with wages had the second strongest association with intrinsic job satisfaction and overall job satisfaction (**Decker, Harris-Kojetin and Bercovitz 2009**). They also found that the higher intrinsic job satisfaction reported by nursing assistants, the lower their intent to leave. Thus, satisfaction with wages affects intent to leave through its direct effect on intrinsic job satisfaction.

Howes surveyed home care workers in a consumer-directed program to investigate the impact of wages and benefits on recruitment and retention. She found that access to health insurance through their job was one of the major reasons why workers took the job and why they stayed (**Howes 2008**). In an earlier article, Howes showed that when the wages of home care workers in San Francisco County were doubled, the retention rates of new workers increased from 39 to 74 percent (**Howes 2005**).

In a survey of 255 CNAs in 15 nursing homes, Bishop and colleagues found satisfaction with benefits was consistently important in nursing assistants' commitment to their jobs (**Bishop et al. 2008**).

The Personal Assistance Services Council of Los Angeles County, which represents over 115,000 In-Home Supportive Services consumer-directed home care workers, commissioned a report on the impact benefit programs have on worker retention and stability. The report found that home care workers enrolled in their employer-sponsored health plan had a higher retention rate (56 percent) than workers who were eligible but not enrolled (45 percent) (**RTZ Associates, Inc. 2005**).

Some studies have not found as strong a link between wages/health insurance and turnover. Parsons et al. examined job satisfaction and turnover among nursing assistants in a statewide sample of Louisiana nursing homes. While the researchers found that pay was the major source of dissatisfaction, a multivariate analysis showed that pay did not affect turnover (**Parsons et al. 2003**).

While low wages and lack of health insurance benefits have a documented influence on direct care worker retention, they are not the only factors having an impact. The next sections look at how culture change, workplace/job design, management practices, trained supervisors, comprehensive training, career opportunities and cultural competence play equally important roles.

B. Overarching Strategy: Culture Change

Culture change is a philosophy of care that emphasizes person-centered care and staff empowerment, built around the concept of home. Culture change practices for staff include many of the non-wage and benefit factors that contribute to retention: comprehensive and expanded trainings, a focus on the relationships between direct care staff and their supervisors, and empowering direct care workers through self-managed work teams or peer-mentoring programs.

How Is Culture Change Defined?

The Pioneer Network, formed in 1997, has been in the forefront of the culture change movement. Its mission is to move aging services away from an institutional model to models that embrace flexibility and self-determination for the person receiving the care.

On its Web site, the Pioneer Network defines culture change as:

"… a national movement for the transformation of older adult services, based on person-directed values and practices where the voices of elders and those working with them are considered and respected. Core person-directed values are choice, dignity, respect, self-determination and purposeful living."

In 2006, the Commonwealth Fund brought together an expert panel to develop a working definition of culture change. This definition was later used in a Centers for Medicare & Medicaid Services-funded project measuring culture change and in the Commonwealth Fund's 2007 National Survey of Nursing Homes (**Colorado Foundation for Medical Care 2006; Doty, Koren and Sturla 2008**)[2]. According to the definition, a culture change nursing home includes the following:

- Resident-directed care and activities
- An environment designed to be a home rather than an institution
- Close relationships among residents, family members, staff and the community
- Work organized to support and empower all staff to respond to residents' needs and desires
- Management that allows for collaborative and decentralized decision making
- Processes that are measurement-based and used for continuous quality improvement

Research is beginning to show the business case for adopting culture change. In an unpublished study, Elliot compared nursing homes participating in the Pioneer Network versus non-participating homes to determine whether there were differences in quality and financial outcomes. She found that those nursing homes that were early adopters of culture change achieved better quality outcomes (as measured by survey citations) and had better financial outcomes (**Elliot 2007, unpublished**).

[2] The 2007 Commonwealth Fund National Survey of Nursing Homes assessed how far along nursing homes are in adopting culture change. For more information about the survey and the results, visit www.commonwealthfund.org/Content/Surveys/2007/The-Commonwealth-Fund-2007-National-Survey-of-Nursing-Homes.aspx

In the Commonwealth Fund's 2007 National Survey of Nursing Homes, Doty and colleagues found the more nursing homes embraced culture change principles, the greater the increase in staff retention and occupancy rates and the greater the decrease in operational costs (**Doty, Koren and Sturla 2008**).

Rabig et al., in a study on four Green Houses© in Mississippi, found staff absenteeism and turnover were lower than in the other nursing facilities operated by the organization (**Rabig et al. 2006**).

C. Overarching Strategies: Workplace/Job Design, Management Practices and Trained Supervisors

Changes in workplace/job design, management practices and supervisory training for direct care worker supervisors have all shown to impact direct care worker satisfaction and retention rates.

A seminal study of the managerial practices that characterize providers with lower turnover and higher retention identified five practices that distinguish these providers (**Eaton 2001**):

- High quality leadership and management, offering recognition, meaning and feedback
- An organizational culture that values and respects nursing staff, especially direct care workers
- Positive human resource practices, including flexibility, training and career ladders
- Thoughtful and effective organization and care practices that help retain staff and build relationships
- Sufficient staffing ratios to allow for the delivery of quality care

Stott et al. looked at the extent to which management practices, designed to increase recruitment and retention of direct care workers, were taking place in 132 providers participating in the Better Jobs Better Care (BJBC)[3] demonstration projects (**Stott et al. 2007**). The researchers looked at:

- Job design, which included participating in care planning, communicating about tasks and feedback
- Direct care worker training/professional development, which included becoming a higher-level direct care worker, a licensed practical nurse, a peer mentor or participating in training/orientation beyond the basic requirements
- Supervisor training and development

Overall, the researchers found that despite the need to recruit and retain direct care workers, these management practices, designed to increase recruitment and retention, were not used consistently across the provider organizations. Providers used job-design practices more frequently than staff training and professional development.

Bowers and her colleagues provided insight into why poor management practices lead direct care workers to leave their job. They conducted in-depth interviews with CNAs at three nursing homes to better understand why they quit (**Bowers, Esmond and Jacobson 2003**). The CNAs confirmed the many factors already established in the literature as causes of turnover: dissatisfaction with organizational policies and practices, training and orientation practices, and low compensation. But it was not these actual policies and practices that led CNAs to leave; it was what these policies and

[3] Better Jobs Better Care (BJBC) was a four-year, $15.5 million research and demonstration grant program, designed to find ways to reduce the turnover rates of direct care workers and improve workforce quality. BJBC was funded by the Robert Wood Johnson Foundation and The Atlantic Philanthropies and was managed by the Institute for the Future of Aging Services at AAHSA.

practices represented to the CNAs—that they were not appreciated, valued or respected by the organization. CNAs pointed to the gap between what their organizations said they valued and what they actually practiced. The CNAs saw their supervisors as the embodiment of the organization's disrespect of them as workers and people, and as such, their relationship with their supervisors was central to turnover.

Supportive and Trained Supervisors

The importance of supervisors to the retention of direct care workers cannot be overstated. Numerous studies have noted that the quality of the supervisory relationship between direct care workers and their nurse supervisors is an essential element to job satisfaction and retention of direct care staff.

According to Stone, "Direct care workers whose work is valued and appreciated by supervisors, and who are listened to and encouraged to participate in care planning decisions, have higher levels of job satisfaction and are more likely to stay in their jobs" (**Stone 2007**).

As part of the evaluation of the five BJBC state demonstration projects, Kemper and his associates surveyed 3,468 direct care staff working with 122 long-term care providers to uncover the single most important thing their employer could do to improve their job as direct care workers. Across the settings (nursing homes, assisted living facilities and home care), workers called for more pay and improved work relationships, especially with their supervisors (**Kemper et al. 2008**).

Bishop et al. investigated whether CNAs were more committed to their job when they felt recognized for their knowledge and perceived their jobs as having greater autonomy and teamwork (**Bishop et al. 2008**). The researchers surveyed 255 CNAs in 15 Massachusetts nursing homes. While satisfaction with wages, benefits and advancement opportunities were all significantly related to nursing assistants' intent to stay on the job, good basic supervision was most important in affecting their job commitment and their intent to stay in their jobs. When nursing assistants perceived their supervisors as respectful, helpful and providing good feedback—in other words as providing good basic supervision—the CNAs were more likely to be committed to their jobs.

In a study using data from the 2004 National Nursing Assistant Survey, Bishop and her colleagues found that nursing homes could increase job satisfaction by supporting good relationships between nursing assistants and their supervisors (**Bishop et al. 2009**).

In another study using the 2004 National Nursing Assistant Survey, Decker and associates found that nursing assistants' assessments of their supervisors had an indirect effect on their intent to leave and a direct correlation with their job satisfaction (**Decker, Harris-Kojetin and Bercovitz 2009**).

Jervis's study of the relationships between nurses and nursing assistants showed that in an urban nursing home, multiple layers of tension brought on by the hierarchical structure and "chain of command" mentality existed between nurses and nursing assistants (**Jervis 2002**). The home's nurses, nursing supervisors and management saw the high nursing assistant turnover rate (77 percent) as the result of nursing assistants' character defects, personal problems and lack of job commitment. By focusing on these aspects of nursing assistants, management avoided looking at the organizational culture and processes that contributed to turnover.

In a study on the recruitment and retention practices of California's not-for-profit

providers, Harahan et al. found that direct care staff felt the charge nurses did not respect them or value their work (**Harahan et al. 2003**). Despite this obvious poor relationship between staff and supervisors, the charge nurses did not perceive themselves as managers and therefore did not see the need for management training.

The nursing assistant workforce development initiative, WIN A STEP UP, achieved its strongest results when paired with the coaching supervision program developed by PHI (**Morgan et al. 2007**). Designed for improving the supervisory skills of direct care worker supervisors, the coaching program helped supervisors support the training nursing assistants received under WIN A STEP UP, assisted them in translating their learning into practice, and improved the relationships between supervisors and nursing assistants.

D. Comprehensive Training

Current direct care worker training requirements long have been viewed as inadequate for the scope and depth of the direct care worker job. The federal government requires nurse aides and home health aides working in Medicare/Medicaid-certified agencies to have 75 hours of initial training. Many states have established additional training requirements, up to 120 hours for nurse aides, but this is still low compared to other service professions (**IOM 2008**). Continuing-education requirements for nurse aides and home health aides are 12 hours per year. Personal and home care aides have no federal training requirements, although several states have established their own.

The IOM report, Retooling for an Aging America: Building the Health Care Workforce, recommends that the minimum federal requirements for CNAs and home health aides be raised to 120 hours and include a demonstration of competence in caring for older adults as part of certification. The report also recommends that states establish minimum training requirements for personal care aides.

A national literature review by the Pennsylvania Intra-Governmental Council on Long-Term Care (PALTC) found that higher levels of training led to increased retention across the long-term care continuum, although this effect was stronger in home health agencies than in nursing homes (**PALTC 2001, as cited in PHI and IFAS 2005**).

Not only do many observers consider the number of required training hours to be insufficient, but they also regard the training itself to be inadequate. In a BJBC-sponsored study of direct care staff in 49 nursing homes, assisted living residences and home health agencies, researchers found that poor training, orientation and continuing education are among the job-related stressors that are significant predictors of job dissatisfaction (**Ejaz et al. 2008**). When these workers across a five-county area of Ohio shared their perceptions and recommendations for training, job orientation and continuing education, 41 percent reported that their initial training had not prepared them or only somewhat prepared them for the job (**Menne et al. 2007**). Forty-two percent felt their job orientation was either not very helpful or only somewhat helpful, and 39 percent felt their continuing education was either not at all or only somewhat useful. The staff who were more satisfied with the quality of their training also had higher job satisfaction and were more likely to stay on the job.

The Menne study included direct care staff recommendations for improving training content and deliver. Training they found the most useful focused on:

- Caring for residents with dementia

- Communicating with residents
- End-of-life issues and coping with grief
- Caring for residents with mental illnesses and problem behaviors
- Resident care skills such as bathing, eating and dressing
- Working with other direct care workers, teamwork and organizing tasks

Staff also wanted to receive their training and education via a more hands-on, experiential and interactive approach.

The Wellspring program, designed to increase the quality of residents' care through enhanced clinical training and empowering certified nursing assistants with interdisciplinary teams, has shown a positive effect on retention rates. A 2002 evaluation showed that over a four-year period, the retention rates for all nursing staff (registered nurses, licensed practical nurses and CNAs) went from 70 to 76 percent in Wellspring homes. Among non-Wellspring homes, retention rates fell from 74 to 68 percent (**Stone et al. 2002**).

An evaluation of another nursing assistant training model, the WIN A STEP UP program, which provides clinical and other types of training, such as being part of a team, showed a modest increase in staff retention (**Morgan and Konrad 2008**). The evaluation also found improved CNA perceptions of nursing care, supportive leadership, team care, career and financial rewards, and providing care to those with dementia.

LEAP (Learn, Empower, Achieve, Produce), a workforce development program, has been found to empower staff, increase retention, and build leadership and communication among CNAs and their supervisors. Current research findings on aging-services providers that have participated in LEAP show a reduction in staff turnover rates of between 38 and 60 percent, an increase in job satisfaction and effectiveness, and a 33 percent decrease in health deficiencies (**Hollinger-Smith 2008, unpublished**).

E. Career Advancement Opportunities

Career advancement opportunities for direct care workers include career ladders and lattices and peer mentoring. These opportunities provide additional training, status and often pay increases. Studies show that the lack of these opportunities is a key reason why workers leave the direct care field.

Brannon et al. studied how job perceptions of the direct care workers participating in the BJBC demonstration projects related to their intent to leave their job (**Brannon et al. 2007**). A total of 3,039 workers from 50 nursing homes, 39 home care agencies, 40 assisted living facilities and 10 adult day services in five states participated in the survey. The researchers found that the perceived lack of opportunity for advancement and the perception of work overload were most significantly related to intent to leave, particularly among home care agency and skilled nursing home staff.

Parsons et al. examined the job satisfaction and turnover among nursing assistants in a statewide sample of nursing homes in Louisiana (**Parsons et al. 2003**). The authors identified the work issues that were the sources of the workers' greatest satisfaction (their relationships with residents) and dissatisfaction (managerial and organizational workforce issues and pay and benefits). The authors found that lower satisfaction was highly associated with turnover, and personal opportunity was the most significant factor related to both job satisfaction and turnover.

The Massachusetts Extended Care Career Ladder Initiative (ECCLI), a career ladder program for direct care staff, was evaluated by the Institute for the Future of Aging Services

and the Gerontology Institute of the University of Massachusetts (**Washko et al. 2007**). The evaluation showed that the career ladders and soft-skills training programs (communication skills, conflict management and teamwork) offered in ECCLI provided the basis for better career opportunities for employees. The authors noted modest and significant turnover reductions in several of the organizations in the study. Administrators reported reduced turnover among staff who participated in ECCLI training, indicating the importance of enrolling new employees in the program.

Peer mentoring also has been shown to address retention problems for both new and seasoned workers. According to Pillemer, 40 to 50 percent of all new nursing assistants left during the first three months on the job (**Pillemer 1996, as cited in PHI 2003**). Some of the reasons included isolation, especially among home health aides, and the realization that their training was inadequate in preparing them for the reality of caregiving work (**PHI 2003**). Peer mentoring provides a new aide with at least one person for support while starting out in a challenging profession, and overall builds relationships among co-workers (**Hegeman et al. 2007**). In a peer-mentor program, seasoned workers can provide support to new staff while growing personally and professionally.

Two studies on Growing Strong Roots, a peer-mentoring program for nursing home CNAs, showed improved retention rates for new CNAs. In the first study, the CNA retention rates increased from 51 to 70 percent during a three-month period. The second study, conducted over a two-year period, measured retention rates at three-month and six-month intervals. At three months, the average retention rates increased from 66 to 77 percent. At six months, the average retention rates increased from 47 to 64 percent (**Hegeman et al. 2007**).

F. Importance of Cultural Competence

Aging-services providers need to address the cultural competence needs of their staff and residents. Almost half of direct care workers belong to racial or ethnic minorities, including 33 percent who are African American and 15 percent who are either Hispanic or other persons of color (**Harahan and Stone 2009**). The racial and ethnic diversity of frontline staff—including an increasing proportion of nursing assistants, home care aides and personal care workers who are foreign-born and may or may not speak English—underscores the need for educational programs that address English literacy. It also shows the need for the more subtle nuances of dealing with a range of cultures in the workplace. Cultural competence needs to be built into training efforts that focus on relational skills between staff and residents/clients and between peers and supervisors, as well as in trainings that address clinical issues (**Stone 2007**).

A study in four California nursing homes found that Filipina licensed vocational nurses were more uncomfortable than black or white nurses in carrying out supervisory responsibilities, or even raising issues to the nursing director that might improve the workplace. Such assertiveness was not part of their cultural norm. The study also uncovered differences between racial and ethnic groups (**Bowers, Stone and Sanders 2007**.)

Allensworth-Davies et al. examined organization cultural competence to determine if it was related to differences in job satisfaction (**Allensworth-Davies et al. 2007**). In four New England nursing homes, researchers asked 135 nursing assistants eight organizational cultural-competence questions.

These questions explored their comfort in the workplace regarding different races or cultures, communication across cultures and the role of management in cross-cultural conflict. The study's findings showed that the nursing assistants' perception of organizational cultural competence was the strongest predictor of their job satisfaction. As the perception of cultural competence increased, job satisfaction also increased.

The researchers suggested that developing and maintaining organizational cultural competence is an important management strategy for increasing job satisfaction and improving staff retention. Managers' focus should be on:

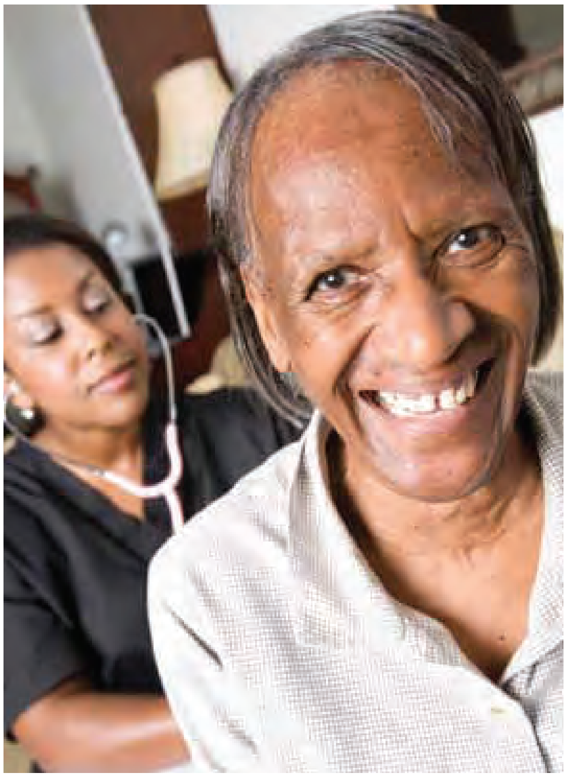
- Improving cross-cultural communication
- Developing and training staff in how to respond to perceived unfair treatment of residents/co-workers due to race/culture
- Involving all levels of staff and residents in culture change activities
- Ensuring that staff are supported in their professional development and receive regular feedback on their performance

In their BJBC-sponsored study, Parker and Geron identified several cultural competence issues that should be addressed in formal orientation and on-the-job training programs (**Parker and Geron 2007**). These included:

- Increasing staff awareness about cultural differences among residents/clients
- Addressing communication issues, particularly related to accents, tone, body language and fluency
- Helping staff to avoid minimizing cultural differences among employees
- Dealing with overtly discriminatory comments, attitudes and actions from staff, residents/clients and families
- Developing specific organizational/ managerial responses to a lack of cultural competence

IV.

Retention Strategies and Programs for Direct Care Workers



A number of programs and strategies incorporating the factors shown to improve retention have been developed and implemented in aging services.

The retention strategies/initiatives and programs highlighted in this section are organized into categories similar to those for the research in Section III, namely:

A. Competitive wages and health insurance benefits

B. Overarching strategy of culture change

C. Overarching strategies of workplace/job design, management practices and trained supervisors

D. Comprehensive training needed to deliver quality care

E. Career advancement opportunities (peer mentoring, career ladders)

F. The importance of cultural competence

The programs selected for this report often included an evaluation that showed a positive impact on direct care worker retention and an improvement in the work environment. This list is not exhaustive. It presents only a few of the many examples of programs and strategies that providers and other long-term care organizations have developed and implemented to increase direct care worker retention.

A. Competitive Wages and Health Insurance Benefits

State and local entities have implemented several initiatives to improve wages and benefits for direct care workers (**Kassner 2006**). These initiatives include wage pass-through legislation, setting wage floors, rate enhancements linked to provider performance goals or targets, living-wage laws, collective bargaining and health insurance proposals specifically targeted at direct care workers.

The 2008 IOM report, Retooling for an Aging America: Building the Health Care Workforce, addressed the problems of low pay and lack of health insurance benefits for direct care staff. The report recommended:

> *State Medicaid programs should increase pay and fringe benefits for direct care workers through such measures as wage pass-throughs, setting floor wages, establishing minimum percentages of service rates directed to direct labor costs and other means (***IOM 2008***).*

The report also supported efforts to address the lack of consistent hours and resulting unstable income of direct care workers, especially home care workers. Cooperative Home Care Associates in Bronx, N.Y., implemented one promising strategy, guaranteed hours, to reduce turnover and vacancy rates (**PHI 2007, as cited in IOM 2008**). According to Steve Edelstein, PHI national policy director, after workers have been employed for three years, Cooperative Associates guarantees 30 paid hours per week even when work hours do not meet that threshold. In exchange, workers must agree to take all assignments, to participate in an on-call pool and be available to work every other weekend. Operating in conjunction with other workforce interventions, the home care agency reduced their turnover to half the national average and enabled their short-hour case workers to expand their hours worked.

Wages

The most prevalent initiative for increasing direct care worker pay has been the wage pass-through, with more than 20 states implementing this mechanism. With a wage pass-through, state Medicaid programs specifically direct a portion of their reimbursement rate to a nursing home or home care agency, toward increasing compensation for direct care staff. Evaluations to date on this approach have shown mixed results on its impact on recruitment and retention. In an analysis of the problem, a brief from PHI and the Institute for the Future of Aging Services (IFAS) points to several key decisions that need to be made up front to improve the effectiveness of wage pass-through programs (**PHI and IFAS 2003**). These decisions include determining:

- The size of the salary increase
- Which staff will be targeted for the increase
- How much flexibility providers have in implementing the program
- Whether provider participation will be optional or mandatory
- What type of accountability will be required
- Whether the wage pass-through will be integrated into the ongoing wage structure
- How and when to educate providers about the program

Health Insurance Benefits

Beginning in 2003, the Centers for Medicare & Medicaid Services (CMS) Demonstration to Improve the Direct Service Community Workforce project undertook several initiatives to create affordable health insurance for direct care workers. In 2003 and 2004, the project awarded five grants to develop and implement programs that test recruitment and retention strategies for direct service workers. CMS set aside more than half the grant funding specifically for projects that addressed health insurance coverage. Five additional grants were awarded in subsequent years. Of the ten grantees, six used all or a portion of their funds to make health care coverage more affordable and/or accessible for direct service workers. The six grantees were located in Indiana, Maine, North Carolina, Virginia, New Mexico and Washington.

A report on the grantees' health coverage interventions provides an overview of how grantees are pursuing these approaches, discusses the key advantages and disadvantages of each, and highlights some of the lessons learned about expanding health coverage to this workforce (**PHI 2006**).

The PHI report, Coverage Models from the States: Strategies for Expanding Health Coverage to the Direct Care Workforce, looks at five broad strategies for expanding health care coverage to direct care workers and gives specific state examples (**PHI 2007**). These strategies are:

- Making employer-based insurance more affordable
- Expanding public insurance coverage
- Establishing coverage through collective bargaining
- Building insurance costs into Medicaid reimbursement
- Assisting workers with health care expenses

In 2005, PHI launched a Health Care for Health Care Workers initiative to advocate for expanding health coverage for workers who provide support and assistance to elders and people living with chronic conditions and/or disabilities. The initiative has produced several statewide studies of insurance coverage for direct care workers, analyses of various state and local efforts, and numerous issue briefs and policy reports. Through the support of Health Care for Health Care Workers and the Direct Care Alliance[4], the state of Maine received an $8.5 million grant from the U.S. Department of Health and Human Services in September 2009 to expand health coverage to Maine's direct care workers. For more information about Health Care for Health Care Workers, contact Carol Regan, national director, (301) 587-1225, CRegan@PHInational.org.

[4] The Direct Care Alliance is a national advocacy organization of direct care workers, committed to advocating for better wages, benefits, respect and working conditions.

B. Overarching Strategy: Culture Change

There are many tools available to assist aging-services organizations in implementing culture change practices. Two Web sites offering a number of resources for providers include the Pioneer Network and the Institute for Caregiver Education.

The Pioneer Network, formed in 1997, calls for a movement away from institutional models to more consumer-oriented models that embrace flexibility and self-determination. This has come to be known as the long-term care culture change movement. The Institute for Caregiver Education is a nonprofit organization dedicated to transforming eldercare from a clinical model to a social model of care through culture change. The Institute offers education and training programs, consultation and seminars to support frontline caregivers.

CMS has shown its support of culture change efforts in recent years and is working with the quality improvement organizations and the Pioneer Network to encourage long-term care providers to adopt culture change practices

In April 2008, CMS and the Pioneer Network co-sponsored Creating Home in the Nursing Home: A National Symposium on Culture Change and the Environment Requirements. The symposium brought together long-term care innovators, regulators, researchers, architects, advocates and public officials to highlight environmental innovations and discuss how to transform nursing home physical environments into home and community within federal regulations and the Life Safety Code . The following day,

stakeholders worked together to develop recommendations.

Because of the recommendations, CMS implemented changes, effective June 2009, to its Guidance to Surveyors for several Quality of Life and Environment sections. These changes include allowing residents to receive visitors 24 hours a day and supporting a home-like environment by encouraging residents to wear their own clothes and determining their own activities and schedules.

Another outcome of the symposium was the creation of a National Life Safety Task Force, convened by the Pioneer Network, which is working to change the Life Safety Code by 2012 to accommodate culture change innovation.

CMS and the Pioneer Network are planning a second symposium, which will focus on how dining initiatives interact with regulations.

On the following pages, five cultural-change tools are described.

Artifacts of Culture Change

Artifacts of Culture Change is a tool nursing homes can use to determine how well they have incorporated culture change into their organizations. It captures a concrete set of changes homes can make to their practices and policies in the process of transforming an institutional culture into one that is person- and staff-centered. The tool was developed by Carmen S. Bowman, Edu-Catering: Catering Education for Compliance and Culture Change in LTC, and Karen Schoeneman, deputy director of the CMS Division of Nursing Homes. Although it is a CMS-developed product, it is not connected to enforcement and is not punitive; no surveyors will collect data using this tool.

The Artifacts of Culture Change tool consists of 79 scored questions that give providers a way to measure their progress and benchmark where they are on the culture change journey. The questions are divided into the following categories:

- Care practices
- Workplace practices
- Environment
- Family and Community
- Leadership
- Outcomes

The Development of the Artifacts of Culture Change includes the Artifacts of Culture Change tool, as well as information on how the tool was created and how to use it.

How to Obtain This Tool

The Development of the Artifacts of Culture Change and the Artifacts of Culture Change itself are available at www.pioneernetwork.net/Providers/Artifacts/.

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Household Matters: A Good Life 'Round the Clock

Household Matters is a toolkit of resources and materials to assist aging-services organizations and others to transform the culture of nursing homes. The toolkit was created by Meadowlark Hills, a continuing care retirement community in Kansas, and Action Pact, Inc., with funding from the Sunflower Foundation and the Kansas Department on Aging.

The toolkit contains the following resources:

- In Pursuit of the Sunbeam: A Practical Guide to Transformation from Institution to Household (hard copy)
- Living and Working in Harmony: A Training Guide for Self-Led Teams (hard copy)
- Creating Home (CD) – a set of policies and procedures shaped for household life. Based on federal regulations, this manual demonstrates that the regulations support culture change principles.
- Living and Working in Harmony (CD) – an integrated human resources system that reflects the values of the household model and provides resources for creating a decentralized organization utilizing self-led teams
- Reflecting on Quality (CD) – a system of team-based continuous quality improvement

The kit also contains three DVDs that provide 10-to-12 minute video clips covering different aspects of culture change, including an orientation to households, person-centered care, creating community, kitchen practices and the dining experience.

How to Obtain This Tool

Household Matters is available from the Pioneer Network for $718. For more information, visit www.pioneernetwork.net/Store/HouseholdMatters/.

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Getting Started: A Pioneering Approach to Culture Change in Long-Term Care Organizations

Getting Started is a handbook for long-term care providers beginning to incorporate culture change principles and practices into their organizations. It is based upon interviews with leaders in long-term care organizations who have been on the journey toward cultural transformation for three or more years. The Pioneer Network partnered with PHI to produce this tool for starting the process of de-institutionalizing services and individualizing care. The Retirement Research Foundation and the Commonwealth Fund provided funding.

The handbook includes personal stories of individuals who have embraced culture change, reviews how to assess an organization's readiness for change, and discusses the importance of examining and realigning values, mission and vision statements.

The handbook includes thirteen training modules, which are designed to introduce culture change values to the entire nursing home community and begin the process of transformation. Each module has detailed facilitator guides and handouts.

How to Obtain This Tool

Getting Started is available from the Pioneer Network for $199. For more information, visit www.pioneernetwork.net/Store/GettingStarted.

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Implementing Change in Long-Term Care: A Practical Guide in Long-Term Care

Implementing Change in Long-Term Care is manual designed to assist aging-services organizations in implementing changes that improve quality. The changes can range from an organization-wide culture change effort to implementing a single practice, such as peer mentoring for direct care workers. The manual was written by Barbara Bowers and associates from the University of Wisconsin-Madison School of Nursing, with funding from the Commonwealth Fund.

One of the manual's overall themes is the importance of involving all staff when implementing any culture change practice. This means going beyond the staff directly impacted by the practice change, as a way of ensuring the change will be more lasting and sustained. The topics covered in the manual include:

- Person-centered care and culture change models
- Leadership
- Developing teams
- Developing staff
- Preparing for change
- Conducting organizational assessments
- Sustaining change and developing accountability systems

Organizations can use the manual's sections in a way that makes the most sense to them. For example, if an organization has already incorporated person-centered care into its practices, but has not developed work teams, it can go directly to that section.

How to Obtain This Tool

Implementing Change in Long-Term Care is available at www.nhqualitycampaign.org/star_index.aspx?controls=resManualForChange.

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Staff Assessment Tool: Person-Directed Care

The staff assessment tool, developed by the Oregon BJBC demonstration project, is designed to assess the person-centered and person-directed care practices and perceptions of long-term care staff. The survey questions focus on five dimensions of person-directed care: personhood, knowing the person, autonomy/choice, comfort and relating to others. Another set of questions addresses organizational and physical environments that support person-directed care practices. The tool is a step toward putting the concepts of person-directed care into practice.

Aging-services providers can use this tool to evaluate how well their staff is meeting person-directed care goals. The survey can directly measure the attitudes and perceptions of staff toward person-directed care and provide feedback on whether true person-directed care is being practiced. It also can help gauge how well the concepts of person-directed care have been internalized. The survey itself can serve to educate staff about what person-directed care looks like and provide guidance to providers who want to change practices.

How to Obtain This Tool

The staff assessment tool is available at www.bjbc.org/content/docs/Staff_PCC_AssessmentTool_Nov2006.pdf.

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C. Overarching Strategies: Workplace/Job Design, Management Practices and Trained Supervisors

The Retention Specialist Program[5]

The retention specialist program, developed by a team of researchers from the Cornell Institute for Translational Research on Aging (CITRA), is a promising and cost-effective model designed to improve CNA retention in aging-services providers.

In this model, a staff person from an aging-services organization is chosen to be a retention specialist, charged with diagnosing and addressing retention problems. The specialist should have the expertise and ongoing management support to address problems of low job satisfaction and turnover. The specialist receives in-depth training and resources focused on implementing a range of proven strategies. These strategies include peer mentoring, career ladders, communication training, recognition and supervision. The specialist also receives the tools necessary to conduct a needs assessment of the organization's retention issues, in order to select the most appropriate retention strategies, establish retention programs and evaluate his or her success.

The CITRA research team conducted a randomized, controlled evaluation study of the program, testing the effects of training retention specialists in 16 nursing homes in New York and Connecticut (**Pillemer et al. 2008**). The researchers found:

- The participating nursing homes experienced an 11-percent decline in turnover over a 12-month period compared to a 3-percent decline in the control group.
- The retention specialist program had a positive effect on general perceptions of the nursing home and specifically on CNAs' assessments of the facility's efforts in the areas of training and attempts to retain staff.
- The position positively affected CNAs' perceptions of the quality of the nursing home administration.

For More Information

A retention specialist toolkit, containing descriptions and links to the evidence-based strategies used in the specialists' two-day training, is available at www.citra.org/wordpress/rsp-tookit.

About the retention specialist evaluation, visit http://gerontologist.gerontologyjournals.org/cgi/content/abstract/48/suppl_1/80.

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[5] Information on the retention specialist program was drawn from a background document in the retention specialist toolkit, http://www.citra.org/wordpress/wp-content/uploads/the-retention-specialist-program.pdf.

Northern New England LEADS Institute

The Northern New England LEADS Institute was a three-year demonstration project to improve the quality of direct care jobs at 12 participating nursing homes and home care agencies in Vermont, New Hampshire and Maine. Launched by PHI, the goal of the Institute was to improve the quality of direct care jobs by providing training and technical assistance to the participating providers.

The LEADS interventions included:

- Training selected staff to deliver peer mentoring and coaching supervision throughout their organization
- Redesigning caregiving practices to be more person-directed through training and technical assistance to supervisors and administrators
- Establishing leadership teams, which included direct care workers, that focused on quality-improvement efforts

A 2008 evaluation showed decreased turnover at sites with strong implementation of coaching supervision and peer mentoring (**PHI 2008, LEADS evaluation**). Specific results included:

- Turnover for direct care workers decreased three to 46 percentage points from 2006 to 2007 for six of the 10 sites (for which there were complete data).
- Two of the three organizations with very strong and sustainable coaching supervision and peer-mentoring programs achieved reductions in both turnover and call-outs.
- Five of the nine organizations with strong implementation of one or more LEADS interventions improved on turnover and/or calls-outs.

For More Information

About the LEADS program and evaluation, visit http://phinational.org/archives/phi-project-finds-less-turnover-with-training/#more-640.

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Staff Stability Toolkit

The Staff Stability Toolkit is designed to serve as a resource for nursing homes seeking to reverse their direct care worker turnover. The toolkit incorporates experiences and lessons learned in more than 400 nursing homes, and applies concepts and practices based on Eaton's work on management's impact on staff turnover (**Eaton 2001**). Strategies and techniques based on Eaton's findings have been successfully piloted in the Vermont BJBC demonstration project, the CMS-funded Improving Nursing Home Culture Pilot, with nursing homes nationally through the quality improvement organizations (QIO) and in New England through workforce development programs.

The toolkit, developed by B & F Consulting under a subcontract with Quality Partners of Rhode Island and funded by the Commonwealth Fund, provides resources that help nursing homes examine fiscal, organizational and management practices that may cause the turnover cycle. The resources include:

- Suggestions on getting started and ways to include all employees in reducing turnover
- Tips on management practices that support stability related to recruiting and hiring, attendance, scheduling, consistent assignment and building leadership
- A "drill-down" tool that helps to gather and analyze data about turnover, absenteeism and financial incentives
- A case study describing how a BJBC nursing home used the drill-down process to identify the root causes of their instability and re-allocate their financial and management resources to support stability.
- Information on how to use training to support stability and improve organizational performance and where to find resources to fund training

How to Obtain This Tool

The Staff Stability Toolkit is available at www.riqualitypartners.org/cfmodules/objmgr.cfm?Obj=NHQ_QIOSharedMaterials&pmid=124&mid=145&cid=145.

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12 Steps to Creating a Culture of Retention: A Workbook

12 Steps to Creating a Culture of Retention is a workbook that offers 12 concrete steps to guide providers in developing excellent recruitment, selection and retention practices—the three key elements necessary to manage long-term care organizations successfully. The 12 steps that frame this workbook, developed by PHI, are based on the principle of "quality care through quality jobs."

Typically, many providers frame the turnover cycle as a "recruitment" problem. **Steps 1 through 4** address recruitment and selection strategies. Following the checklists and using information in the resources and attachments will help organizations enrich their recruitment processes. They will be able to clarify the qualities of their ideal worker, determine how to attract those ideal workers and ensure that their screening processes help them select quality caregivers.

While recruitment and selection are critical to building a culture of retention, the ultimate problem is not just finding the right staff; it is also keeping the right staff. **Steps 5 through 12** focus on creating a workplace culture of retention. This means beginning with an effective orientation program and following through with a variety of initiatives that enhance relationships, skills and voice for all staff.

Additional resources from PHI supporting retention efforts include:

- Attachments (included at the back of the workbook)
- Published references, available for free download from www.phinational.org
- Best-practice reports and other materials posted at PHI's National Clearinghouse on the Direct Care Workforce, www.PHInational.org/clearinghouse
- Unpublished resources, available by contacting info@PHInational.org

How to Obtain This Tool

12 Steps to Creating a Culture of Retention: A Workbook is available at http://phinational.org/training/resources/recruitment-retention/.

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LEAP

LEAP: Learn, Empower, Achieve, Produce is a workforce development program focusing on key components that stabilize the long-term care workforce and empower staff to become partners with residents in creating a person-directed culture of care. LEAP, created by Mather LifeWays Institute on Aging, is built on the philosophy that a stable, empowered workforce is the critical element in achieving a transformed culture.

LEAP offers several different programs to aging-services providers:

LEAP 101 provides long-term care communities with the tools to begin their culture change transformation. This program focuses on three key areas that are important first steps to implementing culture change in the community: person-directed care, primary/consistent assignments and peer mentoring.

LEAP for Long-Term Care Communities (LEAP LTC) has been successful in increasing retention of nursing home staff, building leadership and communication among CNAs and their supervisors, and improving the quality of life and satisfaction among residents and families. The program consists of two modules. Module 1 trains nurse managers and charge nurses in leadership, role modeling and team-building skills, as well as clinical gerontological skills. Module 2 trains CNAs in person-centered care, communication skills, team building, mentoring and career building. Current research findings on aging-services providers that have participated in LEAP LTC show a 48 percent reduction in voluntary terminations, a 62 percent reduction in involuntary terminations, a 35 percent reduction in nursing staff vacancies and a 33 percent decrease in health deficiencies (**Hollinger-Smith 2008, unpublished**).

LEAP LTC has received the following awards:

- 2004 Award for Excellence in Clinical Practice from the American Association of Homes and Services for the Aging
- 2004 Healthcare and Aging Award from Pfizer Medical Humanities Initiative and the American Society on Aging
- 2003 Extendicare Foundation Award for Innovations in Retention and Promotion of Nursing Assistants in Long-Term Care

LEAP for Senior Living builds on the principles of person-directed care as they relate to assisted living, independent living and continuing care retirement communities. Its unique interdisciplinary approach focuses on cultural/ethnic diversity among staff members and residents, plus strategies for effective communication, team building and understanding normal aging issues. When the community is operating as a whole integrated system, job satisfaction and staff retention increase, resulting in greater resident and family satisfaction.

For More Information

About the LEAP family of programs, visit www.matherlifeways.com/leap.

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Coaching Supervision: Introductory Skills for Supervisors in Home and Residential Care

Coaching Supervision: Introductory Skills, developed by PHI, is a training program that builds the coaching skills of supervisors of direct care workers who provide care in home and residential settings. The training introduces supervisors to a new model of supervision based on relationship-building and communication skills. With these skills, supervisors can help workers solve problems more effectively and improve work performance.

The training is divided into seven modules, designed to be taught over two days. In the training, supervisors explore four key skills:

- Active listening: Focused listening, paraphrasing and asking open-ended questions to understand a problem from the worker's perspective
- Self-management: Pulling back from emotional responses that can get in the way of listening
- Self-awareness: Being conscious of one's own perspective as one of many
- Presenting the problem: Without judgment, holding workers accountable for job performance

The curriculum is based on adult-learning principles and includes examples of real-life situations, role-plays, small-group work and interactive presentations. The curriculum includes learning objectives, activities, questions for discussion, all necessary handouts and is available for either home care or nursing home settings.

This training program has been accredited by the American Nurses Credentialing Center, a subsidiary of the American Nurses Association.

For More Information

About PHI's Coaching Supervision program, visit http://phinational.org/training/our-services/coaching-supervision/.

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Pathways to Leadership

Pathways to Leadership is a research-based, peer-mentoring education program designed to improve the management, leadership and communication skills of nursing home charge nurses, including licensed practical nurses and registered nurses. Administered by the Foundation for Long Term Care with funding from the New York State Department of Health Dementia Program and the Fan Fox and Leslie R. Samuels Foundation, the program is designed to:

- Improve the management, leadership and communication skills of long-term care charge nurses, especially as they relate to dementia
- Teach positive skills related to managing a long-term care unit
- Improve the retention rates of charge nurses
- Create a caring community of staff and residents on each unit

The program can be implemented in one of two ways:

- **Model 1** (mentoring program for new charge nurses) – selecting the best charge nurses and training them to mentor newly hired charge nurses
- **Model 2** (mentoring program with existing charge nurses) – selecting two experienced nurses, who have participated in the training, to mentor each other (**Hegeman et al. 2007**)

The program consists of three elements: (1) three-and-a-half hour formal and mandatory administrative and coordinator training, (2) an initial two-day train-the-trainer training in peer mentoring and (3) booster sessions to reinforce content with special emphasis on coaching supervision and applying learned skills to the care of residents with dementia.

The two-day training covers:

- Peer-mentoring skills
- Leadership skills
- Communication skills
- Management skills, including conflict management, handling criticism, time management and delegation
- Dementia knowledge
- The importance of compassion
- Problem solving

Retention rates of new charge nurses and existing charge nurses who participated in the program were tracked prior to mentoring and at three, six and nine months after the mentor training. On average, the nursing homes saw a 15-percentage-point increase in the retention rates, (Information accessed online at Complimentary Train-the-Trainer Program: "Pathways to Leadership," Foundation for Long Term Care, www.nyahsa.org/foundation/swf_doc_host.cfm?rrp=/foundation/n00003225.swf)

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LVN LEAD (Leadership Enrichment and Development)

LVN LEAD is a leadership training program designed to help licensed vocational nurses (LVNs) be more effective leaders and supervisors of frontline care workers. The Institute for the Future of Aging Services (IFAS) developed, piloted and evaluated this program with Aging Services of California and the University of Wisconsin, Madison School of Nursing.

LVN LEAD is intended to help LVNs become better prepared to fill their roles and responsibilities as charge nurses and team leaders, and provide what is usually missing from their formal and continuing education. The program was based upon current research, as well as input from focus groups with LVNs and direct care workers and interviews with nursing facility administrators and interested stakeholders. The training provides LVNs with new skills and competencies in supervision, communication, critical thinking, problem solving, coaching and conflict resolution. It includes culturally competent methods of supervising a diverse workforce.

IFAS is in the process of creating an online version of the training.

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D. Comprehensive Training

The training programs listed below are examples of workforce initiatives and training programs for direct care workers that have shown improvements in retention. Some focus on specific topics such as dementia and palliative care. Others include a more comprehensive approach and include other workforce initiatives and components, such as teamwork and building relationships between direct care workers and supervisors.

The Wellspring Program

Wellspring is a quality improvement model created in Wisconsin by an alliance of 11 nonprofit nursing homes. LifeSpan Network, a mid-Atlantic senior provider association and AAHSA state association, now manages Wellspring. The model offers education, guidance and tools to assist nursing homes in implementing culture change. The primary focus of the program is to strengthen clinical and managerial skills of staff, empower residents and frontline staff, and create a high quality of life for residents.

On its Web site, the Wellspring program states its core principles:

- Care decisions need to take place at the level closest to the resident.
- All staff need a knowledge base to equip them to participate in decision making.
- An empowered workforce increases resident and employee satisfaction and reduces staff turnover.

Key elements of the Wellspring alliance model include:

- An **alliance** of eight to 12 nursing homes in the same geographic area committed to participating in the program and working together
- **Clinical education modules** of the best practices and new developments in clinical practice in eight quality areas: physical assessment, elimination/continence, behavior management, skin care, accident prevention/restraint reduction, restorative care, nutrition and coaching/mentoring
- **Culture transformation educational modules** equipping staff to create a home-like environment and engage and empower residents
- A **nurse consultant**, with extensive long-term care experience and who is shared by alliance members, develops training materials and teaches staff how to apply nationally recognized clinical guidelines
- **Care resource teams** that are interdisciplinary self-directing, non-hierarchical teams that receive training in a specific area of care and are responsible for teaching other staff at their respective facilities
- **Wellspring coordinator –** a registered nurse who links all the elements of the program together, involves all departments within a nursing home, and networks among staff across homes to share what works and what does not on a practical level
- **Empowerment of all nursing home staff** to make decisions affecting the quality of resident care and the work environment
- **Continuous reviews**, by CEOs and all staff, of performance data on resident outcomes and environmental factors relative to other nursing homes in the Wellspring alliance (**Stone et al. 2002; Reinhard and Stone 2001**)

In addition, Wellspring offers customized education and consultation to individual nursing homes that want to launch a culture change initiative.

A 2002 evaluation showed that the retention rates for all nursing staff (registered nurses, licensed practical nurses and CNAs) went up from 70 to 76 percent among Wellspring homes. Among non-Wellspring homes, retention rates fell from 74 to 68 percent (**Stone et al. 2002**).

For More Information

About the Wellspring program, visit www.lifespan-network.org/beacon_wellspring.asp.

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WIN A STEP UP Program

WIN A STEP UP is a workforce intervention program proven to upgrade the skills of nursing assistants in nursing homes, increase their career commitment and job satisfaction, and provide rewards and recognition to participants. WIN A STEP UP developed as a partnership between the North Carolina Division of Health Service Regulation and the University of North Carolina Institute on Aging.

WIN A STEP UP is based on three principles:

- **Education:** Education is essential for quality service in long-term care and builds competence and self-esteem in the workforce.
- **Compensation:** Real concern about direct care workers must be reflected in their paychecks and benefits.
- **Commitment:** All parties who receive benefits from the program should formally agree to contribute to it and be held accountable for performance.

In WIN A STEP UP, nursing assistants complete a 36-hour curriculum covering clinical and interpersonal topics, such as infection control, being part of a team and dementia care. A core feature of the program is that it requires commitment from the nursing assistant, the nursing home and the program staff. The nursing assistant agrees to attend the classes and remain employed at the facility for an agreed upon amount of time. The facility agrees to commit staff time to completing the program and to distribute a retention bonus or wage increase to nursing assistants upon completion.

The program provides the curriculum, the educational incentives to nursing assistants per class and a $75 retention bonus to participants who complete the program. It also includes supplementary training for nursing assistant supervisors in active-listening and problem-solving skills, as well as how to foster an environment of mutual respect.

Dill et al. studied the impact of WIN A STEP UP on direct care staff turnover rates (**Dill, Morgan and Konrad 2009**). By analyzing the data from 2002 to 2006, the authors found the nursing homes participating in the program were 15 percent more likely to have below-average turnover than non-participating homes.

Morgan and Konrad reported improved teamwork between nurses and nursing assistants, improved nursing care, and more satisfaction with career and financial rewards. The program was most successful when it was paired with PHI's two-day coaching supervision training for nurse supervisors (**Morgan and Konrad 2008**). In Morgan et al., the researchers identified several factors that influenced the translation of learning into practice—use of adult-learning principles, role-plays and on-the-floor exercises, clearly written modules, the training taking place at the employees' workplace and on the organizations' time, and management buy-in and support (**Morgan et al. 2007**).

In 2004, the U.S. Department of Health and Human Services identified WIN A STEP UP as one of three programs nationwide proven to be effective in reducing nursing aide turnover. In 2007, WIN A STEP UP was selected as one of two finalists for the Rosalynn Carter Caregiving award.

For More Information

About WIN A STEP UP, visit www.winastepup.org/.

About the WIN A STEP UP evaluation, visit http://gerontologist.gerontologyjournals.org/cgi/content/abstract/48/suppl_1/71.

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Competence with Compassion™
A Universal Core Curriculum for Direct Care Workers in Long-Term Care

Competence with Compassion is a 60-hour universal core curriculum training created and tested by the BJBC Pennsylvania demonstration project. The training is geared toward helping new non-certified direct care workers across all long-term care settings learn the person-centered, relationship-building and direct-care skills that result in better care and a better job. It was created in response to what direct care workers said they needed to provide better care.

The curriculum is divided into six modules, each focused on a different type of consumer and long-term care setting. Each module begins with a consumer telling his or her life story and explaining why he or she needs assistance. The training is based on adult-learning principles with students learning through role-plays, small groups and demonstrations of the skills they have learned. Two Pennsylvania area agencies on aging have endorsed the training for new workers. The training package includes an instructor manual, participant-training book, slides and handouts.

How to Obtain This Tool

Competence with Compassion is available for sale from CARIE (Center for Advocacy for the Rights and Interests of the Elderly) at http://carie.verveinternet.com/store.

Cost:

Training package, including printed format and CD – $225

Training package, printed copy only – $175

Training package, CD format only – $150

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Providing Personal Care Services to Elders and People with Disabilities

Providing Personal Care Services to Elders and People with Disabilities is an adult learner-centered, competency-based curriculum for personal care workers. The Personal Care Services curriculum, developed by PHI, is designed to meet three major goals:

- To help participants develop the core competencies needed to provide person-directed personal care in a range of long-term care settings
- To introduce potential workers to the different long-term care settings
- To lay the foundation for further training as nurse assistants and/or home health aides

The curriculum is divided into 20 three-and-a-half-hour modules and one seven-hour module, for a total training time of 77 hours. **Modules 1 and 2** are an orientation to the work of personal care workers and to key concepts of direct care. The modules also include an introduction to the various settings of direct care work: home care, assisted living, personal care homes, adult day services and nursing homes.

Modules 3 through 8 address the knowledge, attitudes and skills essential in all settings. These include infection control, body mechanics, body systems and common diseases, working with elders, respecting differences and communication skills. **Modules 9 through 19** show how to apply these foundational areas of knowledge, attitudes and skills when working with individual consumers using a person-directed approach to providing care. Participants learn how to assist with activities of daily living (ADLs) for various types of consumers—both elders and independent adults with physical disabilities—through case scenarios and role-plays that focus on consumer profiles in the range of long-term care settings.

Modules 20 and 21 wrap up the training by considering issues affecting consumers and workers across the range of work settings. These issues include mental illness or developmental disability, abuse and neglect, consumers' and workers' rights, the importance of work-life balance, time management and stress management.

The Personal Care Services curriculum can be used in two ways. As a stand-alone curriculum, it can train workers who provide personal care services in people's homes or in assisted living or other residential facilities. It also can serve as a first level of training to prepare workers for jobs in nursing facilities and home health care agencies.

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CareWell: Training Compassionate and Skilled Caregivers

CareWell is a 40-hour training program for direct care workers who work in home health and adult day and residential care. It was developed by the BJBC Vermont demonstration project and was based on the research of best practices nationally. Provided in eight classes, the training program focus is on four main topics: providing care, developing caregivers, providing safety and building relationships.

The program integrates these topics in a skill-based, highly interactive format. Throughout the curriculum, technical skills, such as body mechanics and infection control, are taught alongside communications skills and setting boundaries. Homemaking and personal care skills are interwoven with cultural diversity and time management. Skills checklists completed in class and worksheets completed at home provide the assessment of skills that are based on clearly defined performance outcomes. CareWell's comprehensive approach helps build self-esteem and confidence for both new and experienced caregivers.

CareWell is facilitated using adult-learning theory. Each class is grounded in real-life case scenarios with interactive activities, practice in a learning lab and work done at home. Professional instructors with experience in physical therapy, RN certification and direct care staff training can facilitate this training program. The CareWell curriculum materials include a participant manual with materials and support information for each class, participant portfolio outcome verification, and worksheets to indicate proficiency of skills and grasp of materials covered during the training. A facilitator's manual includes an introduction to CareWell, the curriculum, principles and course flow, facilitator planning charts for each class and PowerPoint slides with detailed notes for each class.

The program can serve as a curriculum for both new and experienced direct care staff. The materials can be integrated into orientation and ongoing training, as well as workforce development initiatives. The training program is a resource that can inform professionals and organizations about effective, best-practice approaches to practical direct care staff training.

How to Obtain This Tool

CareWell is available at www.bjbc.org.

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Beyond Basics in Dementia Care

Beyond Basics in Dementia Care is a specialized training to help direct care providers develop effective strategies and new skills in providing care for people with dementia. It was developed by the BJBC Vermont demonstration project with input from recognized Vermont trainers in dementia care. The training is a 12-hour, three-session continuing-education course for experienced licensed nursing assistants and personal care assistants. The course covers the foundation of the nature (pathology) of dementia, managing behaviors and the environment for effective caregiving.

The training program combines lecture, interactive discussion, learning activities, question/answer periods and on-the-job application of the new skills with self-evaluation and peer feedback. The curriculum includes participant assignments, agendas, core concepts, evaluation forms and a course director handbook. It also includes information on portfolios that can be used to gather and present evidence of the participants' competency in their knowledge and clinical skills, information to present at the beginning of classes and a template certificate.

The training is geared to professional direct care workers who are currently involved in dementia care in any setting or who hope to develop expertise in dementia care.

How to Obtain This Tool

Beyond Basics in Dementia Care is available at http://www.bjbc.org/tools.asp.

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Beyond Basics in Palliative Care

Beyond Basics in Palliative Care is designed to give direct care providers specialized training in understanding the challenges of palliative care and the strategies for improving care for people with chronic and life-threatening illnesses. The training was developed by the BJBC Vermont demonstration project and incorporates materials from many sources, but especially from the Hospice and Palliative Care Nurses' Association and the Vermont Ethics Network. It is a 12-hour, three-session continuing-education course for experienced licensed nursing assistants and personal care attendants. The course covers issues related to the care of people with chronic illness, pain/symptom management, communicating with the resident/client and family, and providing comfort care at the end of life.

The training program combines lecture, interactive discussion, learning activities, question/answer periods and on-the-job application of the new skills with self-evaluation and peer feedback. The curriculum includes participant assignments, curriculum outline, evaluation forms and a course director handbook. It also includes information on portfolios that can be used to gather and present evidence of the participants' competency in their knowledge and clinical skills, information to present at the beginning of classes and a template certificate.

The intended audiences for this curriculum are direct care providers currently involved in palliative care in any setting, caregivers seeking to develop expertise in palliative care, and direct care providers who want more training to understand the issues and upgrade their professional skills.

How to Obtain This Tool

Beyond Basics in Palliative Care is available at http://www.bjbc.org/tools.asp.

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Geriatric Resource Specialist Program

The Geriatric Resource Specialist Program is an 80-hour training program that teaches leadership and clinical knowledge and skills to interdisciplinary teams of both licensed and unlicensed staff to improve their care of residents/clients. The program was developed and is offered by the Central Plains Geriatric Education Center, housed at the Landon Center on Aging, University of Kansas Medical Center.

The participants are required to take a set of core courses and a defined number of elective courses, which use adult-learning principles, to obtain the continuing-education credits and the program certificate. The core courses, usually held over six days, include leadership, mentoring and interpersonal skills, as well as clinical knowledge and skills. Participants are required to take 20 hours of elective courses ranging from oral and eye diseases and conditions, fall prevention, dementia and health literacy. Both core and elective courses are based on evidence-based care and practices.

Each team identifies an aspect of care that needs improvement and then develops and presents recommendations for changing this care practice.

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E. Career Advancement Opportunities

Peer Mentoring

Growing Strong Roots

Growing Strong Roots is a peer-mentoring program for new CNAs working in nursing homes. Developed by the Foundation for Long Term Care (FLTC), the program was implemented across 31 diverse nursing homes in New York state. The goals of the program are to:

- Improve retention of new CNAs by improving orientation processes that reflect the facility's values
- Improve the quality of care by teaching the value of caring and reinforcing skills and behaviors (**Hegeman et al. 2007**)

Each facility participating in the program has a project coordinator to oversee the planning and implementation of the mentor program. The project coordinator and the administrator are required to attend a three-hour orientation.

Supervisor orientation: Supervisors attend a one-hour orientation, intended to build understanding and support for the project and to ensure that supervisors do not see the program as diminishing their authority.

Mentor selection: Each facility designs its own mentor-selection process, although FLTC recommends using a transparent process. FLTC also recommends involving the union, if the facility has one, and establishing a formal reward system for mentors.

Peer-mentoring training: The peer-mentoring training is in a train-the-trainer format, consisting mostly of interactive exercises, role-plays and case studies (**Hegeman 2005**). Mentors are taught to:

- Identify the roles of the mentor (role model, social support, tutor and peer resource)
- Describe how a positive attitude sets the tone for the social and professional integration of mentees into the facility
- Demonstrate the use of effective communication skills, including listening skills, communication blockers and enablers, and conflict management
- Describe ways to use leadership skills to recognize and manage potential conflicts and solve problems
- Recognize situations in which information or guidance is needed from other sources and be able to access those resources
- Use mentoring skills in simulated mentor-mentee sessions

Mentor-mentee relationship: Mentoring is intended to supplement, not replace or duplicate, the usual training of new CNAs. Each mentor and mentee pair, who work together on the same shift and unit, have an active relationship for four or more weeks, with the greatest intensity in the beginning of the relationship. The mentor is a role model, social support, tutor and peer resource for the mentee. Mentors model correct clinical skills, positive attitudes and time management.

Mentors receive additional pay for time spent as mentors. Some facilities also provide non-cash incentives, such as an extra week of paid vacation or not having to work on weekends when mentoring.

Mentor booster session: Three separate three-hour sessions review the skills introduced in the training program and encourage participants to share challenges and successes in mentoring, as well as to suggest solutions to challenges.

Two studies on Growing Strong Roots have documented that nursing homes implementing the program improved the retention rates of their new CNAs. In the first study, the CNA retention rates increased from 51 to 70 percent during a three-month period. The second study was conducted over a two-year period and measured retention rates at three-month and six-month intervals. At three months, the average retention rates increased from 66 to 77 percent. At six months, the average retention rates increased from 47 to 64 percent (**Hegeman et al. 2007**).

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Peer Mentoring: A Workshop Series for Direct Care Workers in Home and Residential Settings

The peer mentoring workshop series is intended to prepare experienced direct care workers in home and residential settings to become peer mentors. It was developed by PHI in cooperation with Cooperative Home Care Associates and CNR Nursing System, both in New York City, and Home Care Associates of Philadelphia. The curriculum focuses on developing self-awareness and interpersonal skills rather than clinical, task-related or teaching skills. The series focuses on three skill areas: leadership, communication and problem solving for direct care workers. Eight modules prepare mentors to:

- Model good caregiving skills
- Model effective communication and problem-solving skills
- Support the mentee to build confidence in his or her abilities
- Give mentees constructive feedback
- Provide mentees with current information about job responsibilities and the workplace

The curriculum is interactive, learner-focused and based on adult-learning principles. The teaching methods include case studies, role-plays, small-group work and interactive presentation. The facilitator's guide includes module goals, learning outcomes, step-by-step activity guides and all necessary handouts. The curriculum can be taught through community college nursing aide programs, advanced training institutes or employer-based in-service programs. The modular format makes the program easily adaptable to fit the needs of many organizations.

The peer mentoring workshop series has been accredited by the American Nurses Credentialing Center, a subsidiary of the American Nurses Association.

For More Information

About the peer mentoring program, visit: http://phinational.org/training/resources/peer-mentoring/.

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Career Ladders and Lattices

Employee PRIDE Program

The Employee PRIDE (Provide Respect, Incentives, Career Development and Education) program was developed by NewCourtland Elder Services, an organization providing long-term care, community services and affordable senior housing in Philadelphia. Employee PRIDE is based on the premise that better training and more advancement opportunities for staff will lead to better care. The program offers scholarship and tuition assistance to meet these goals.

The Ladder of Opportunity is the cornerstone of the program, whereby any employee can advance in the nursing field. A career ladder provides training for a CNA to become a CNA II and a CNA specialist.

All CNAs who have been with NewCourtland for one year, have had no disciplinary action taken against them and have completed the CNA training program automatically become CNA IIs. The next step of the ladder, a CNA specialist, involves submitting an application, a brief essay and references from a supervisor and the director of nursing. Once accepted, the CNA has three months of classroom and clinical experiences in nutrition, wound prevention, skin care and restorative care. Once these requirements are completed, the employee becomes a CNA specialist and receives a raise of $1 an hour. Job duties remain essentially the same, but CNA specialists take on some additional tasks, such as documentation follow-up. They also may sit on facility committees addressing matters such as wounds and falls. Others may serve on the Peer Review Committee, acting as preceptors for new CNAs and helping them during orientation. (Information accessed online, July 30 from National Clearinghouse on the Direct Care Workforce, www.directcareclearinghouse.org/practices/r_pp_det.jsp?res_id=52810.)

The program also offers scholarships, tuition reimbursement and stipends for employees to further their education to become licensed practical nurses or registered nurses. They can obtain bachelor or master of science degrees in nursing.

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Geriatric Nursing Assistant Specialist (GNAS)

The Geriatric Nursing Assistant Specialist training program was developed by Genesis HealthCare for their CNAs working in their skilled nursing and assisted living settings. The training provides a career ladder for CNAs and is an effective retention tool.

The objectives of the program are to:

- Give CNAs an opportunity to expand their skills and uses them in creative ways
- Provide CNAs with a career ladder that includes a pay increase
- Demonstrate that CNAs can have an important impact on the management and delivery of care
- Increase all staff's respect and understanding of the CNA role
- Increase CNA motivation and retention

A CNA is eligible to apply to the program when he or she has met the following criteria: six months tenure, above-average performance evaluations, a positive attitude. Interested candidates need to write a one-page essay to apply.

Once selected, CNAs participate in 100-108 hours or training, through the following six training modules:

- Introduction to communication: Includes active listening, verbal and non-verbal communication, conflict resolution, and customer service.
- Anatomy and physiology: Emphasizes the changes associated with aging. Participants learn to communicate with other professionals using technical language.
- Cognition, death and dying: Teaches signs and symptoms of dementia, techniques for dealing with difficult behaviors, stages of grief, detection of vital signs that signal impending death, and counseling family members of dying patients.
- Common disorders of the elderly: Covers signs and symptoms of Parkinson's disease, diabetes, dementia and congestive heart failure.
- Care process minimum data set (MDS), therapeutic recreation, and rehab skills: Covers rehabilitation techniques and documentation.
- Advanced communication: Teaches how to serve as role models and mentors and to participate in the CNA interview process.

CNAs who complete the first three modules receive a 50-cent increase in their hourly pay. When they have completed all six modules, their pay is increased $1.25 per hour and they receive the designation of GNAS.

These specialists' new responsibilities can include overseeing the orientation program mentoring entry-level nursing assistants, serving as a CNA liaison on the performance improvement committee, monitoring CNA tasks during daily quality rounds or greeting new families and residents.

The program has increased CNA retention and shown to be cost effective.

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Registered Apprenticeship Programs

The Council of Adult and Experiential Learning (CAEL) and PHI, with funding from the Office of Apprenticeship in the U.S. Department of Labor (DOL), created the following career lattice programs for direct care workers, which DOL certifies as registered apprenticeship programs.

Nurse Career Lattice Program

CAEL created a nurse career lattice program to increase the number of CNAs, licensed practical nurses and registered nurses working in acute and long-term care. The program was piloted in nine states and was developed through partnerships with employers, local workforce investment boards, colleges and DOL Apprenticeship offices. Persons entering the program learn through clinical and didactic training both in the classroom and on the job. Participants can become CNAs, if they are not already, and then move laterally by becoming mentors, medication aides or specialists in geriatrics, restorative care or dementia. CNAs also can choose to become LPNs through a series of courses at educational institutions or online. LPNs can continue their training, and those who wish, can become RNs. The program has increased retention, reduced recruitment costs and decreased worker shortages (**CAEL 2005 and 2008, as cited in IOM 2008**).

CAEL has developed a toolkit, How Career Lattices Help Solve Nursing and Other Workforce Shortages in Healthcare, to assist governments, health care employers and others to create their own career lattice programs. The toolkit includes the model components, lessons learned from the pilots and steps for creating a program.

For More Information

About the nurse career ladder program and for access to the toolkit, visit www.cael.org/healthcare.htm.

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Home Health Aide Registered Apprenticeship Program

PHI developed the Home Health Aide (HHA) Registered Apprenticeship Program with support from a U.S. Department of Labor grant.

The HHA curriculum is competency-based and allows apprentices to gain basic skills and advance in specialty areas, such as hospice, palliative care, geriatrics, disabilities, mental illness, dementia and mentoring. Apprentices are expected to demonstrate competence in basic home care skills and in at least two specialties. Apprentices receive interim credentials and pay raises as they complete parts of the program. Experienced home health aides serve as peer mentors and support entry-level apprentices.

Five home health agencies in Pennsylvania, Indiana and Michigan have implemented the HHA program as pilots. PHI provides support to the sites, including program design, recruitment strategies and tools, an on-the-job peer-monitoring program, training and competency assessment, outcome measurement and fund-raising help. Goals for the traditional apprenticeship program include improving retention, increasing job satisfaction, improving customer satisfaction and enhancing the collaboration with the public workforce system. All five agencies continue to enroll and train new apprentices and advance those still enrolled in the program.

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F. The Importance of Cultural Competence

Cultural Competence

Getting Ready: Focusing on Cultural Competence in Long-Term Care Organizations

Getting Ready is a resource to assist long-term care providers in addressing the cultural competence issues in their organization. It was developed by Victoria Parker and associates at Boston University under the BJBC grant program. Based on the results of a cultural competence research study, the guide includes:

- The lessons learned from an assessment of the cultural competence issues faced by 10 nursing homes and the subsequent interventions designed to help the homes address these issues
- Discussions on what diversity, culture and culture competence mean and how these factors can influence the experience of residents/clients and those who care for them
- The importance of assessing staff's attitudes, behaviors and policies towards diversity and their readiness to change
- A resource directory listing consulting firms, training and assessment tools, and organizations that can help

Long-term care organizations can use this resource to guide them in the process of assessing their staff's concerns, attitudes, perceptions and behaviors around cultural-competency issues between staff, between staff and managers, and between staff and residents.

How to Obtain This Tool

Getting Ready is available at www.bjbc.org/content/docs/GettingReady.pdf.

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Creating Solutions: Handling Culturally Complex Situations in a Long-Term Care Setting

Creating Solutions is a training guide that assists nursing home staff in discussing culturally complex situations that may arise in a facility. Developed by Victoria Parker and associates at Boston University under the BJBC grant program, the guide contains multiple case studies, discussion questions, and handouts for use in both orientation and in-service trainings.

The objectives of the guide are to:

- Increase awareness of cultural issues at the workplace
- Increase communication about issues that arise due to cultural differences
- Build a support network for direct care workers
- Increase supervisor and management understanding of direct care workers' experiences in dealing with cultural differences
- Provide direct care workers with possible strategies to use in the face of these difficult situations

The guide is organized into two sections. The first section, designed to be used during orientation, includes case studies, small-group discussions, role-plays and strategies that can be used in similar situations. The second section is designed to be used during an in-service, but also can be used during an orientation, if time allows. This section uses the BJBC video, Stand Up and Tell Them: Views from the Frontline in Long-Term Care, and the accompanying discussion guide as part of the training. It includes a case study, small-group discussions and strategies workers can use when facing similar situations.

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V.

Additional Tools and Resources

A. Clearinghouses

National Clearinghouse on the Direct Care Workforce

The National Clearinghouse is a national online library that provides information on the direct care workforce, including retention strategies and programs. Initially developed by PHI and the Institute for the Future of Aging Services, with funding from the U.S. Department of Health and Human Services, the clearinghouse includes government and research reports, news, issue briefs, fact sheets, training manuals and how-to guides.

The best practices database offers profiles of programs implemented by providers, educators, workers and community organizations. The database topics include best practices on wages and benefits, workplace culture and empowerment, recruitment and retention, education and training, supervision, career advancement and care practices.

In addition, the Clearinghouse publishes original research and analysis, including fact sheets, state-specific information, an annual survey of state initiatives on the direct care workforce, a list of direct care worker associations and Quality Care/Quality Jobs, a free weekly online newsletter.

For More Information
About the National Clearinghouse, visit www.directcareclearinghouse.org/index.jsp.

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National Direct Service Workforce Resource Center

The National Direct Service Workforce Resource Center provides information and resources that support efforts to improve recruitment and retention of direct service workers who help older adults and people with disabilities live independently and with dignity. These workers include direct support professionals, personal care attendants, personal assistance providers, home care aides, home health aides and others.

The Center's resources include a Web-based clearinghouse, technical experts and training tools that cover the full range of direct service populations. The database has information, resources, policy research and other materials on a variety of topics, such as recruitment, retention, training, supervision and consumer direction, from leading organizations in the field of direct service workforce policy. The technical experts include The Lewin Group, PHI, the Institute for the Future of Aging Services, the University of Minnesota's Research and Training Center on Community Living, the Westchester Consulting Group and the Annapolis Coalition on the Behavioral Health Workforce.

The DSW Resource Center is funded and supported by the Centers for Medicare & Medicaid Services under the U.S. Department for Health and Human Services.

For More Information

About the National Direct Service Workforce Resource Center, visit www.dswresourcecenter.org/.

Better Jobs Better Care

Better Jobs Better Care (BJBC) was the largest national initiative dedicated to improving workforce quality and reducing high vacancy and turnover rates among direct care staff across the spectrum of long-term care settings. The four-year, $15.5 million research and demonstration program, funded by the Robert Wood Johnson Foundation and The Atlantic Philanthropies, provided grants for five state demonstration and eight applied research and evaluation projects.

The state demonstration grants, awarded to Iowa, North Carolina, Oregon, Pennsylvania and Vermont, created statewide coalitions comprised of key long-term care stakeholders, including providers, workers and consumers. The coalitions worked with state and local officials to develop and implement policy changes and provider practice interventions at the state or regional level. Grantees addressed a broad range of long-term care, health care, labor, education policy and practice issues that affect the quality of the direct care worker's job.

Applied research and evaluation grants were intended to generate practical, empirically-based knowledge about the strategies and practices that work best to attract and retain a high-quality direct care workforce. The grantees provided findings on potential pools of new workers, the training that direct care workers and their supervisors want and need, the importance of supervisors, the effect management practices have on job satisfaction, and the impact competitive wages, benefits and career opportunities have on attracting and retaining workers.

BJBC has developed a series of tools and resources that provide the key research findings and lessons learned from the program. These include:

A Crisis With a Solution: Tools and Resources for Transforming the Long-Term Care Workforce
A catalogue highlighting the tools and resources develop by the BJBC grantees. It includes dementia and palliative care trainings, occupational profiles for entry-level and advanced frontline staff, and an online manual of evidence-based retention strategies.

A Crisis With a Solution: Transforming the Long-Term Care Workforce, video
A video featuring Robyn Stone, PhD, executive director of IFAS and co-creator of BJBC, sharing real stories from providers who used the lessons learned from BJBC to empower their employees and transform their work with older adults.

Solutions You Can Use: Transforming the Long-Term Care Workforce
A report outlining key BJBC research findings and what they mean to long-term care providers. Findings include information on where to find new pools of direct care workers, what interventions improve staff retention and how to develop cultural competence in your organization.

Better Jobs Better Care: New Research on the Long-Term Care Workforce
A special issue of The Gerontologist presents BJBC's research findings and Pennsylvania State University's evaluation of the demonstration projects. http://gerontologist.gerontologyjournals.org/content/vol48/suppl_1/.

Better Jobs Better Care was directed and managed by the Institute for the Future of Aging Services (IFAS), the applied research arm of American Association of Homes and Services for the Aging (AAHSA). Technical assistance was provided in partnership with PHI (formerly the Paraprofessional Healthcare Institute).

For More Information

About BJBC, visit www.bjbc.org.

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B. Recruitment

Occupational Profile for Entry-Level Direct Care Workers Across Aging Services

The BJBC Oregon demonstration project developed the occupational profile for uncertified and unlicensed entry-level direct care workers. It includes a comprehensive task list, skills definitions and skill levels for entry-level direct care workers across the aging-services continuum of community-based care, including home care, residential care and assisted living. The profile creates a common language around the knowledge, tasks, generic or foundation skills, and the proficiency levels needed for those skills required by entry-level direct care workers. A person-centered/directed-care philosophy statement also is included.

Long-term care providers can use the occupational profile to guide them in recruiting, hiring and training entry-level direct care workers who are not certified or licensed. They also can use the profile to develop job descriptions, interview questions and evaluation criteria for job performance and training. Job developers and policy makers can use the profile to create programs supporting job seekers, job changers, employers and incumbent workers in all care settings, including community-based care.

How to Obtain This Tool

The occupational profile is available at http://www.bjbc.org/tools.asp.

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Occupational Profile for Advanced Direct Care Workers Across Aging Services

The BJBC Oregon demonstration project developed the occupational profile for uncertified and unlicensed advanced direct care workers. It includes a comprehensive task list, skills definitions and skill levels for advanced direct care workers across the aging-services continuum of community-based care, including home care, residential care and assisted living. The profile creates a common language around the knowledge, tasks, generic or foundation skills, and the proficiency levels needed for those skills required of advanced direct care workers. A person centered/directed-care philosophy statement also is included.

Long-term care providers can use the occupational profile to guide them in recruiting, hiring and training advanced direct care workers who are not certified or licensed. They also can use the profile to develop job descriptions, interview questions and evaluation criteria for job performance and training. Job developers and policy makers can use the profile to create programs supporting job seekers, job changers, employers and incumbent workers in all care settings, including community-based care.

How to Obtain This Tool

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C. State Initiatives for Direct Care Workers

Extended Care Career Ladder Initiative (ECCLI)

The Extended Care Career Ladder Initiative (ECCLI) is a comprehensive workforce training program in Massachusetts, designed to enhance the quality and outcomes of resident/client care and to address the recruitment/retention problems of direct care workers through career ladders and other training initiatives. Nursing homes and home health agencies can apply for ECCLI funds through a competitive, multiple-round grant program. The Commonwealth Corporation, a quasi-government entity, manages ECCLI.

The career-ladder programs implemented in ECCLI typically involve creating incremental steps with associated modest wage increases. Career-ladder steps focus training on both clinical skills (e.g., nutrition, skin assessment and transferring) and soft skills (e.g., communication, mentoring and leadership). Some organizations have developed a bridge to a nursing component that prepares employees to enter a college-level nursing program. The majority of organizations rely on partner organizations (community colleges, regional employment boards and workforce investment boards) to provide training in order to access expertise appropriate to their goals. Many have partnered with other long-term care organizations for joint training activities. These partnerships expand the training capacity beyond what each organization could provide on its own and allow employees to experience a connection to the larger long-term care community.

In addition to career ladders, ECCLI funds other training and educational opportunities that reach a wider audience of employees. Frontline workers can be trained in communication skills, conflict management and teamwork. Supervisors can learn basic supervision and capacity building in order to incorporate new CNA or home health aide skills into work practices. English as a Second Language classes provide many employees with educational opportunities to improve their language skills or to prepare for college-level classes. Mentor training is often part of a career ladder in nursing homes and part of soft-skills training for home health aides. Permanent resident assignments and training on person-centered care are among the initiatives introduced to foster culture change practices.

The Institute for the Future of Aging Services and the Gerontology Institute of the University of Massachusetts conducted a qualitative evaluation of ECCLI (**Washko et al. 2007**). Their findings showed that the career ladders and soft-skills training programs provided the basis for better career opportunities for employees. The positive impact of ECCLI seemed to result from the breadth of training opportunities offered for all employees, tailored to organizations' needs. Improvements in communication, clinical skills, teamwork, respect and self-confidence, wages, retention and recruitment, organizational culture and practice change, and resident/client quality of care and quality of life were observed in most of the participating organizations.

For More Information

About ECCLI, visit www.commcorp.org/eccli/index.html.

About the ECCLI evaluation, visit www.aahsa.org/uploadedFiles/IFAS/Publications_amp;_Products/eccli_final_report(1).pdf.

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North Carolina New Organizational Vision Award (NC NOVA)

NC NOVA, developed by the BJBC North Carolina demonstration project, is a voluntary, specialty state license that recognizes providers for workplace excellence through their investment in their workers and improved workplace culture.

NC NOVA standards fall under four major areas or domains: supportive workplaces, training, career development and balanced workloads. North Carolina providers must have an operating license in good standing to apply for the NC NOVA designation. The Carolinas Center for Medical Excellence (CCME), the North Carolina quality improvement organization, reviews the applications and sends out a review team to conduct an on-site review. The team interviews direct care workers and supervisors to ensure consistency between the information in the application and the programs at the organization. If the CCME deems a provider has met the program's standards and requirements, the North Carolina Department of Health Services Regulations issues the special license, which is good for two years.

The state legislature established NC NOVA as a statewide program effective Jan. 2007. The state helps to administer the program, track the license and advertise the program. The next goal for the program is to tie NC NOVA designation to labor enhancement funds or some reimbursement differential, which is consistent with the workforce recommendations in the 2001 Institute of Medicine's Long-Term Care Task Force Report.

For More Information

About NC NOVA, visit www.ncnova.org.

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COVID-19

Disparities in COVID-19-Associated Hospitalizations

Racial and Ethnic Health Disparities

Updated Nov. 11, 2021

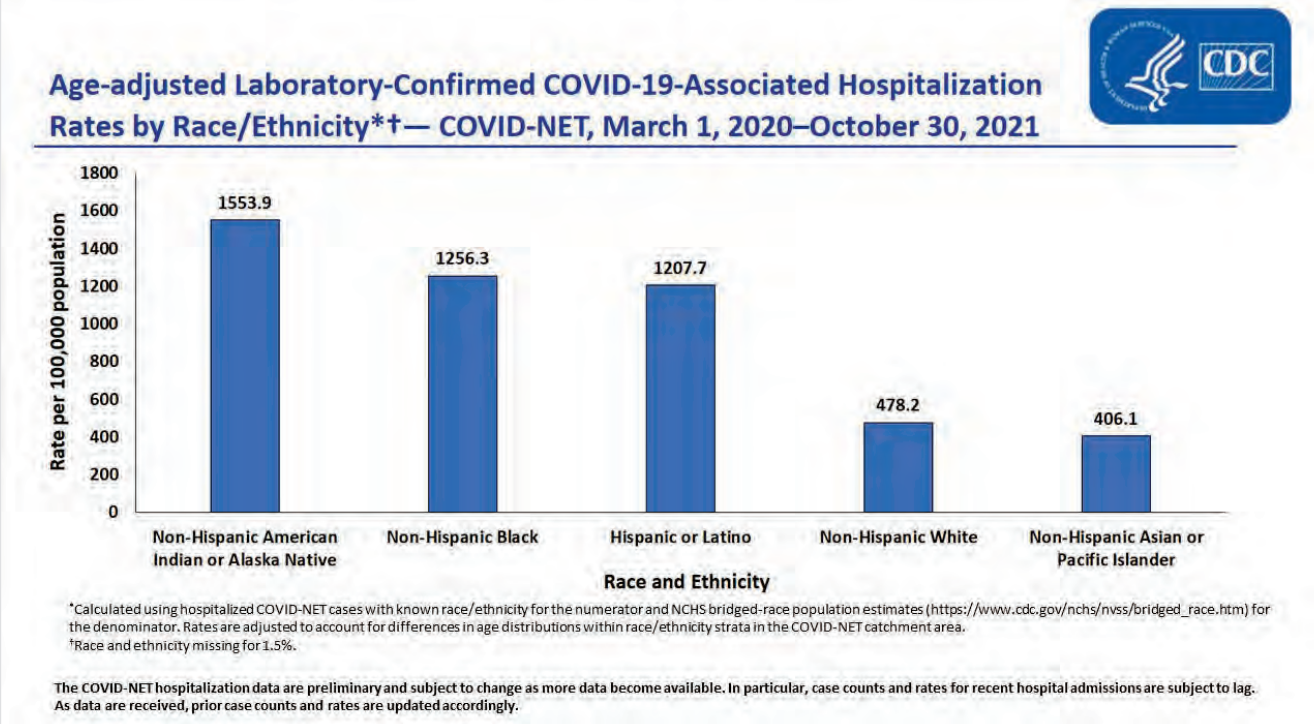
Why are some racial and ethnic minority groups disproportionately affected by COVID-19? The following links provide specific information about underlying health and social inequities that put many racial and ethnic minority groups at increased risk of getting sick, having more severe illness, and dying from COVID-19.

Conditions in the places where people live, learn, work, play, and worship affect a wide range of health risks and outcomes, such as COVID-19 infection, severe illness, and death. These conditions are known as social determinants of health. Long-standing systemic health and social inequities have put many people from racial and ethnic minority groups at increased risk of severe illness from COVID-19.

An important source of data for laboratory-confirmed COVID-19-associated hospitalizations is CDC's COVID-19-Associated Hospitalization Surveillance Network (COVID-NET). COVID-NET provides demographic and clinical information on COVID-19-associated hospitalizations, including age group, sex, race and ethnicity, underlying health conditions, interventions, and outcomes. COVID-NET comprises 99 counties in the 14 states participating in the Emerging Infections Program and the Influenza Hospitalization Surveillance Project; covering approximately 10% of the U.S. population. The age-adjusted hospitalization rates and distribution of characteristics among people hospitalized, including underlying medical conditions and outcomes, by race and ethnicity can be used to identify racial and ethnic disparities and inform potential strategies to reduce disparities.

Age-adjusted Laboratory-Confirmed COVID-19-Associated Hospitalization Rates by Race and Ethnicity — COVID-NET, March 1, 2020–October 30, 2021

Among laboratory-confirmed COVID-19-associated hospitalized cases, more than 90% have information on race and ethnicity. There are differences in age-adjusted hospitalization rates by race and ethnicity. Age-adjusted rates allow for comparisons across groups by accounting for the different age distributions within each racial and ethnic group. Non-Hispanic American Indian or Alaska Native, non-Hispanic Black, and Hispanic or Latino people have higher hospitalization rates compared with non-Hispanic Asian or Pacific Islander and non-Hispanic White people.



[JPG - 144 KB]

*Calculated using hospitalized COVID-NET cases with known race/ethnicity for the numerator and NCHS bridged-race population estimates (https://www.cdc.gov/nchs/nvss/bridged_race.htm) for the denominator. Rates are adjusted to account for differences in age distributions within race/ethnicity strata in the COVID-NET catchment area.

†Race and ethnicity missing for 1.5%.

The COVID-NET hospitalization data are preliminary and subject to change as more data become available. In particular, case counts and rates for recent hospital admissions are subject to lag.

As data are received, prior case counts and rates are updated accordingly.

Hospitalization rates differ by age group and race and ethnicity group. The table below includes hospitalization rates and rate ratios for five racial or ethnic minority groups by age. Racial and ethnic minority groups have disproportionately higher hospitalization rates among every age group, including children aged younger than 18 years. The rate ratios compare the rate for each of these groups relative to the rate for non-Hispanic White people. For example, a rate ratio of 2.0 means that the group has a rate that is 2 times higher than the rate for non-Hispanic White people. In general, all racial and ethnic groups included in the table had higher hospitalization rates than non-Hispanic White people across almost every age category.

Hospitalization Rates per 100,000 population by age and race and ethnicity — COVID-NET, March 1, 2020–October 30, 2021

Age Category	Non-Hispanic American Indian or Alaska Native		Non-Hispanic Black		Hispanic or Latino		Non-Hispanic Asian or Pacific Islander		Non-Hispanic White	
	Rate[1]	Rate Ratio[2,3]	Rate[1]	Rate Ratio[2,3]	Rate[1]	Rate Ratio[2,3]	Rate[1]	Rate Ratio[2,3]	Rate[1]	Rate Ratio[2,3]
0—17 years	105.2	**3.1**	101.2	3.0	97.0	2.8	35.6	1.0	34.3	1.0
18—49 years	1216.4	**5.2**	767.7	3.3	831.6	3.6	212.9	0.9	223.3	1.0
50—64 years	2350.2	**3.5**	1947.4	3.3	1862.7	2.8	599.0	0.9	669.4	1.0

Age Category	Non-Hispanic American Indian or Alaska Native		Non-Hispanic Black		Hispanic or Latino		Non-Hispanic Asian or Pacific Islander		Non-Hispanic White	
65+ years	3608.5	**2.2**	3473.8	2.1	3121.6	1.9	1281.3	0.8	1643.5	1.0
Overall rate[4] (age-adjusted)	1553.9	**3.2**	1256.3	2.6	1207.7	2.5	406.1	0.8	478.2	1.0

[1] COVID-19-associated hospitalization rates by race and ethnicity are calculated using COVID-NET hospitalizations with known race and ethnicity for the numerator and NCHS bridged-race population estimates for the denominator.

[2] For each age category, rate ratios are the ratios between crude hospitalization rates within each racial and ethnic group and the crude hospitalization rate among non-Hispanic White persons in the same age category.

[3] The highest rate ratio in each age category is presented in bold.

[4] Overall rates are adjusted to account for differences in age distributions within race and ethnicity strata in the COVID-NET catchment area; the age strata used for the adjustment include 0–17, 18–49, 50–64, 65-74, 75-84 and 85+ years.

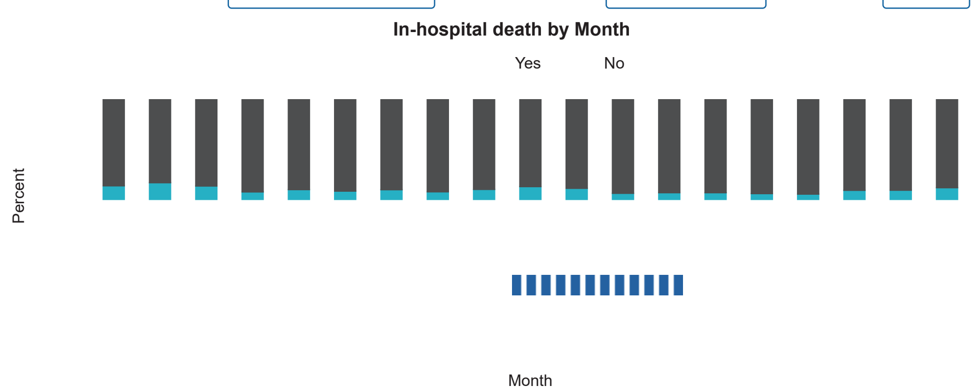
Characteristics of COVID-19-Associated Hospitalizations

The interactive graph below has three menu selections. The first menu includes selecting to view data on the percent of patients hospitalized with COVID-19, or the percent of patients who required mechanical ventilation, required treatment in an intensive care unit, or who died in the hospital by race and ethnicity, age, or sex). Another selection option is to view data on underlying medical conditions (such as asthma, diabetes, obesity or symptoms at admission to the hospital (such as cough, fever/chills, or sore throat) by race and ethnicity, age, or sex. The last selection option is to view data on discharge diagnosis (such as pneumonia, acute respiratory failure, or acute renal failure) are also available by race and ethnicity, age, or sex.

Characteristics of COVID-19-Associated Hospitalizations

Includes data from March 1, 2020 – September 30, 2021

Display by Major Category Interventions/outcomes **and Sub-Category** In-hospital death **stratified by** Month



1. COVID-NET hospitalization data are preliminary and subject to change as more data become available. In particular, case counts and rates for recent hospital admissions are subject to delay. As data are received each week, prior case counts and rates are updated accordingly.
2. White, Black, Asian/Pacific Islander and American Indian/Alaska Native all represent non-Hispanic ethnicity groups; Other includes persons in multiple race categories and persons for whom race is unknown.
3. All data presented, including demographics (age, sex, race and ethnicity), interventions and outcomes, underlying medical conditions, signs/symptoms at admission, vaccination status, and discharge diagnoses are restricted to sampled and completed cases with non-missing data reported during March 1, 2020 – September 30, 2021. Due to the sampling methodology for adults aged ≥18 years, counts and unweighted percentages are only presented for demographic data. Weighted percentages are presented for intensive care unit admission, mechanical ventilation, in-hospital death, underlying medical conditions, signs/symptoms at admission, and discharge diagnoses.
4. Vaccination status was obtained by matching hospitalized cases to state-based immunization information systems (IIS) data. Vaccination data are only available for 13 of 14 states.

Technical Notes

1. COVID-NET hospitalization data are preliminary and subject to change as more data become available. In particular, there may be a lag in hospitals reporting recent case counts and rates for hospital admissions. As data

are received each week, prior case counts and rates are updated according to the reported date of hospital admissions.

2. The denominator for each underlying condition and characteristic data (except for intensive care unit, mechanical ventilation, in-hospital mortality, and discharge diagnoses) is the total number of patients with non-missing data for that condition or characteristic. The denominator for intensive care unit, mechanical ventilation, in-hospital mortality, and discharge diagnoses is restricted to cases who are no longer hospitalized and who have complete medical chart reviews. These data will be updated each week as additional chart reviews are completed.
3. White, Black, Asian/Pacific Islander and American Indian/Alaska Native all represent non-Hispanic ethnicity groups. The “other” race and ethnicity category includes people in multiple race categories and people for whom race is unknown.

Evidence from the literature

Findings from other published studies are consistent with COVID-NET data. Across several studies, most found a higher percent of hospitalized patients were non-Hispanic Black or Hispanic or Latino people than non-Hispanic White people.

Race or Ethnicity Group	Percent of hospitalized COVID-19 patients Median [Range]	# of Studies Reporting
Black	44% [15–81%]	7 [1,2,3,4,5,6,7]
Hispanic or Latino	36% [3–48%]	4 [1,2,3,4]
White	16% [11–72%]	6 [1,2,4,5,6,7]

Notes: Studies reporting data on percent of hospitalized patients by race and ethnicity included people of all ages. These studies analyzed race and ethnicity differently; two studies analyzed the variables separately (racial categories could be Hispanic or Latino or non-Hispanic) and five studies analyzed the variables in a single variable (racial categories were non-Hispanic). Data were inadequate to assess potential differences in percent of hospitalized COVID-19 patients for American Indian and Alaska Native people, Native Hawaiian and other Pacific Islander people, and people who identify with more than one race. Therefore, data for these groups are not reported.

Acute kidney injury has been a common outcome among patients hospitalized with COVID-19. One study found that among patients hospitalized with COVID-19, 37% developed acute kidney injury. Among those with acute kidney injury, 35% died compared with 16% of all patients hospitalized with COVID-19. Acute kidney injury was more likely among Black patients than White patients. [8]

Severe illness from COVID-19 is disproportionately affecting children and adolescents from racial and ethnic minority groups. Multisystem inflammatory syndrome in children (MIS-C) is a rare but severe condition that occurs approximately 2–4 weeks after the onset of COVID-19 in children and adolescents. MIS-C disproportionately affects children and adolescents from racial and ethnic minority groups. [9, 10] More than 70% of reported cases have occurred among children who are Hispanic or Latino or non-Hispanic Black. Data are routinely monitored and updated here.

To prevent severe illness from COVID-19, we need to work together to address inequities in the social determinants of health that increase risk of severe illness from COVID-19 for racial and ethnic minority groups. We must also ensure that everyone has fair and just access to COVID-19 vaccination. Learn more about what we can do to move towards health equity and about what CDC is doing to address COVID-19 Vaccine Equity for Racial and Ethnic Minority Groups (cdc.gov).

To explore additional information and data related to COVID-19 health and vaccination disparities, please visit the Health Equity and Vaccine Equity landing pages within the CDC COVID Data Tracker.

Related Pages

› COVID-NET: A Weekly Summary of U.S. COVID-19 Hospitalization Data

- COVIDView: A Weekly Surveillance Summary of U.S. COVID-19 Activity
- COVID-19 Information for Pediatric Healthcare Providers

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Summary

What is already known about this topic?

Residents of long-term care facilities (LTCFs) and health care personnel (HCP) who work in these facilities were prioritized for early COVID-19 vaccination. Achieving high coverage in this setting is critical to preventing additional outbreaks.

What is added by this report?

During March 2021, 300 LTCFs reported COVID-19 vaccination coverage for their HCP. COVID-19 vaccination coverage was highest among physicians (75.1%) and lowest among aides (45.6%). Vaccination coverage among aides was lower in facilities located in zip code areas with higher levels of social vulnerability.

What are the implications for public health practice?

Additional efforts to improve LTCF immunization practices, build confidence in COVID-19 vaccines, and promote COVID-19 vaccination are needed.

Tables

Table 1

Table 2

References

Related Materials

PDF [89K]

Residents of long-term care facilities (LTCFs) and health care personnel (HCP) working in these facilities are at high risk for COVID-19–associated mortality. As of March 2021, deaths among LTCF residents and HCP have accounted for almost one third (approximately 182,000) of COVID-19–associated deaths in the United States (*1*). Accordingly, LTCF residents and HCP were prioritized for early receipt of COVID-19 vaccination and were targeted for on-site vaccination through the federal Pharmacy Partnership for Long-Term Care Program (*2*). In December 2020, CDC's National Healthcare Safety Network (NHSN) launched COVID-19 vaccination modules, which allow U.S. LTCFs to voluntarily submit weekly facility-level COVID-19 vaccination data.* CDC analyzed data submitted during March 1–April 4, 2021, to describe COVID-19 vaccination coverage among a convenience sample of HCP working in LTCFs, by job category, and compare HCP vaccination coverage rates with social vulnerability metrics of the surrounding community using zip code tabulation area (zip code area) estimates. Through April 4, 2021, a total of 300 LTCFs nationwide, representing approximately 1.8% of LTCFs enrolled in NHSN, reported that 22,825 (56.8%) of 40,212 HCP completed COVID-19 vaccination.[†] Vaccination coverage was highest among physicians and advanced practice providers (75.1%) and lowest among nurses (56.7%) and aides (45.6%). Among aides (including certified nursing assistants, nurse aides, medication aides, and medication assistants), coverage was lower in facilities located in zip code areas with higher social vulnerability (social and structural factors associated with adverse health outcomes), corresponding to vaccination disparities present in the wider community (*3*). Additional efforts are needed to improve LTCF immunization policies and practices, build confidence in COVID-19 vaccines, and promote COVID-19 vaccination. CDC and partners have prepared education and training resources to help educate HCP and promote COVID-19 vaccination coverage among LTCF staff members.[§]

LTCFs voluntarily reported HCP COVID-19 vaccination data using the NHSN COVID-19 vaccination modules through April 4, 2021. Coverage was assessed among LTCF HCP, stratified by job category (denominator).[¶] Vaccinated HCPs (numerator) were those who were vaccinated at the facility or had documentation of receipt of COVID-19 vaccination elsewhere. The module

required responses for the total number of HCP and their COVID-19 vaccinations status; subtotals by job categories were optional. Facilities were included for analysis only if they had reported nonzero values for the number of HCP and their vaccination status by every job category in the most recent weekly report submitted through NHSN during March 1–April 4, 2021. Reported HCP job categories were 1) physicians and advanced practice providers (residents, fellows, advanced practice nurses, and physician assistants); 2) therapists (respiratory, occupational, physical, speech, and music therapists, and therapy assistants); 3) ancillary services employees (environmental, laundry, maintenance, and dietary services); 4) nurses (registered nurses and licensed practical/vocational nurses); 5) aides (certified nursing assistants, nurse aides, medication aides, and medication assistants); and 6) other HCP (personnel not included in the preceding categories, including contract staff members, students, and other nonemployees).

Vaccination coverage for aides, the largest HCP category, was further assessed by social indicators within the zip code area of the LTCF, including median income and percentage of adults belonging to racial and ethnic minority groups, percentage living in poverty, and percentage without a high school diploma; social indicator data were obtained from the 2019 American Community Survey.** Tertiles (higher, moderate, and low) were calculated for each indicator based on the national distribution of zip code areas; facilities in the corresponding zip code area were assigned to each tertile. Because this was a convenience sample, with likely intra-facility or locality clustering in vaccination behavior, confidence intervals were not calculated, nor was statistical testing for percentages performed. One LTCF was excluded from this analysis because a corresponding zip code area was missing. Data were downloaded for analysis on April 7, 2021, and all analyses were conducted using SAS statistical software (version 9.4; SAS Institute). This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[††]

During March 1–April 4, a total of 1,898 LTCFs voluntarily reported HCP COVID-19 vaccination data, including 300 (16%) facilities from 47 states[§§] that reported numbers for HCP and vaccination status for every job category in the most recent weekly report submitted through NHSN (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/108137). Among 40,212 HCP from these LTCFs, 22,825 (56.8%) had completed COVID-19 vaccination (Table 1). In this convenience sample, the group with the highest percentage of reported fully vaccinated HCP were physicians and other advanced practice providers (75.1%), followed by therapists (69.2%), ancillary services employees (58.5%), nurses (56.7%), and aides (45.6%). Coverage was 68.5% among other HCP not reported in these categories (e.g., students and contractors). The proportion of persons who declined COVID-19 vaccination ranged from 11.1% among physicians to 33.2% among aides. Reported recent COVID-19 infections ranged from 0.7% among physicians to 3.0% among aides. The percentage of aides who were completely vaccinated was lower among those working in facilities located in zip code areas with higher proportions of ethnic and racial minorities (43.5% versus 50.5%), lower household median income (40.5% versus 48.1%), higher poverty (42.4% versus 49.2%), and lower high school completion (42.2% versus 49.3%) (Table 2).

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Discussion

In March 2021, data from a convenience sample of 300 LTCFs across the United States indicated disparities in HCP COVID-19 vaccination coverage, with a 30 percentage-point difference in coverage between physicians and other advanced practice providers (75.1%) and aides (45.6%). Among aides, lower vaccination coverage was observed in those facilities located in more socially vulnerable zip code areas. Together, these data suggest that vaccination disparities among job categories likely mirror social disparities in general as well as disparities in the surrounding communities. These findings suggest that vaccination promotion and outreach efforts focused on socially vulnerable and marginalized groups and communities could help address inequities (*4*).

One concern is that nurses and aides in this sample, who have the most patient contact, had the lowest vaccination coverage. COVID-19 outbreaks have occurred in LTCFs in which residents were highly vaccinated, but transmission occurred through unvaccinated staff members (*5*). This finding also has equity implications: national data indicated that aides in nursing homes are disproportionately women and members of racial and ethnic minority groups, with median hourly wages of $13–$15 per hour[¶¶] (*6*); aides are also more likely to have underlying conditions that put them at risk for adverse outcomes from COVID-19 (*7*). As vaccination was made available on site and lower vaccination rates reflected higher declination rates, vaccine hesitancy might have been an important contributor to undervaccination in these facilities.

The finding that vaccination coverage among aides was lower among those working at LTCFs located in zip code areas with higher social vulnerability is consistent with an earlier analysis of overall county-level vaccination coverage by indices of social vulnerability (*3*); however, similar patterns among LTCF staff members are notable because on-site vaccination removed a number of barriers to vaccination, including travel, scheduling, and need to take time off from work.

The findings in this report are subject to at least five limitations. First, facilities included in this analysis had completed a series of optional fields in a voluntary NHSN COVID-19 vaccination module. The 300 facilities presented represent <2% of the >17,000 LTCFs enrolled in NHSN; thus, the findings from this nonprobability–based convenience sample are not generalizable to all LTCFs. Second, LTCFs reported aggregate weekly data, preventing person-level analysis (e.g., by race/ethnicity) and possibly resulting in duplication of reports, if, for example, HCP work at multiple facilities. Third, data on staff member numbers and numbers vaccinated were self-reported by LTCFs and were not independently validated. Fourth, excluding LTCFs reporting zero values might exclude LTCFs with no vaccine coverage (as opposed to nonreporting), thus inflating the estimated vaccination coverage. Finally, this analysis captured vaccination patterns during March 2021, when most facilities had completed on-site vaccination through the federal pharmacy program. Increasing availability and acceptance of COVID-19 vaccinations in subsequent months might have resulted in higher coverage. However, higher staff member turnover in some job categories, including aides, relative to other job categories, might lead to changes in vaccination coverage.

Low vaccination coverage among LTCF staff members highlights disparities across HCP groups, and in the surrounding communities. Additional efforts are warranted to improve LTCF immunization policies and vaccination practices, build HCP confidence in COVID-19 vaccines, and encourage vaccination among persons who have been economically or socially marginalized. On May 11, 2021 the Centers for Medicare & Medicaid Services (CMS) published an interim final rule requiring LTCFs to educate HCP on COVID-19 vaccines, offer vaccination, and report vaccination status to NHSN*** (*8*). CDC and partners have prepared education and training resources to help educate HCP and promote vaccination coverage among LTCF staff members.[†††] Finally, LTCFs could consider best practices from influenza campaigns, which found that employer vaccination requirements were associated with the highest vaccination coverage (*9*).

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* https://www.medrxiv.org/content/10.1101/2021.05.14.21257224v1

† Completed COVID-19 vaccination was defined as 2 doses of Pfizer-BioNTech or Moderna or 1 dose of the Janssen (Johnson & Johnson) COVID-19 vaccines. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

§ https://www.cdc.gov/vaccines/covid-19/toolkits/long-term-care/index.html

¶ https://www.cdc.gov/nhsn/forms/57.219-p.pdf

** https://www.census.gov/programs-surveys/acs

†† 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

§§ No LTCFs were included from Delaware, Minnesota, or Montana.

¶¶ https://phinational.org/wp-content/uploads/2020/01/Its-Time-to-Care-2020-PHI.pdf

*** CDC and CMS data are available at the following: https://www.cdc.gov/nhsn/covid19/ltc-vaccination-dashboard.html and https://data.cms.gov/covid-19/covid-19-nursing-home-data

††† https://www.cdc.gov/vaccines/covid-19/toolkits/long-term-care/index.html

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TABLE 1. COVID-19 vaccination coverage of health care professionals, by job category, in 300 long-term care facilities reporting to the National Healthcare Safety Network — United States, March 1–April 4, 2021

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HCP job category	No. of HCP	No. (%) Fully vaccinated	No. (%) Declined vaccination	No. (%) Recent SARS-CoV-2 infection
Aides*	12,670	5,778 (45.6)	4,204 (33.2)	382 (3.0)
Ancillary services employees†	9,116	5,337 (58.5)	2,374 (26.0)	172 (1.9)
Nurses§	8,622	4,887 (56.7)	2,359 (27.4)	196 (2.3)
Therapists¶	3,028	2,095 (69.2)	527 (17.4)	51 (1.7)
Physicians and advanced practice providers**	1,284	964 (75.1)	142 (11.1)	9 (0.7)
Other HCP††	5,492	3,764 (68.5)	794 (14.5)	78 (1.4)
All staff members	**40,212**	**22,825 (56.8)**	**10,400 (25.9)**	**888 (2.2)**

Abbreviation: HCP = health care personnel.

* Certified nursing assistants, nurse aides, medication aides, and medication assistants.

† Environmental, laundry, maintenance, and dietary services.

§ Registered nurses and licensed practical/vocational nurses.
¶ Respiratory, occupational, physical, speech, and music therapists, and therapy assistants.
** Physicians, residents, fellows, advanced practice nurses, and physician assistants.
†† Personnel not included in the preceding categories, including contract staff members, students, and other nonemployees.

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TABLE 2. COVID-19 vaccination coverage among aides,* by selected social vulnerability metrics and tertile — United States, March 1–April 4, 2021

Return

Social vulnerability metric	Vulnerability tertile, no. vaccinated/total (%)		
	Higher	Moderate	Low
Percentage in racial/ethnic minority group†	2,794/6,416 (43.5)	2,379/5,056 (47.1)	605/1,198 (50.5)
Median income§	1,245/3,072 (40.5)	1,843/4,005 (46.0)	2,690/5,593 (48.1)
Percentage living in poverty¶	1,865/4,397 (42.4)	1,705/3,783 (45.1)	2,208/4,490 (49.2)
Percentage without high school diploma**	1,577/3,739 (42.2)	1,997/4,460 (44.8)	2,204/4,471 (49.3)

* Certified nursing assistants, nurse aides, medication aides, and medication assistants.
† Higher vulnerability tertile: zip code areas with >17.4% persons belonging to racial/ethnic minorities; moderate: 17.4%–96.0%; low: <4.0%.
§ Higher vulnerability tertile: zip code areas with household median income ≤$48,770; moderate: median income >$48,770 through ≤64,741; low: median income >$64,741.
¶ Higher vulnerability tertile: zip code areas with >15.5% of households living under the federal poverty line; moderate: 15.5%–8.1%; low: ≤8.0%.
** Higher vulnerability tertile: zip code areas with >13.6% of persons aged ≥25 years without a high school diploma or equivalent; moderate: 13.6%–6.9%; low: <6.9%.

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View suggested citation

Summary

What is already known about this topic?

Residents of rural communities are at increased risk for severe COVID-19–associated morbidity and mortality. In September 2020, COVID-19 incidence (cases per 100,000 population) in rural counties surpassed that in urban counties.

What is added by this report?

COVID-19 vaccination coverage was lower in rural counties (38.9%) than in urban counties (45.7%); disparities persisted among age groups and by sex.

What are the implications for public health practice?

Disparities in COVID-19 vaccination access and coverage between urban and rural communities can hinder progress toward ending the pandemic. Public health practitioners should collaborate with health care providers, pharmacies, employers, faith leaders, and other community partners to identify and address barriers to COVID-19 vaccination in rural areas.

Figures

Figure 1

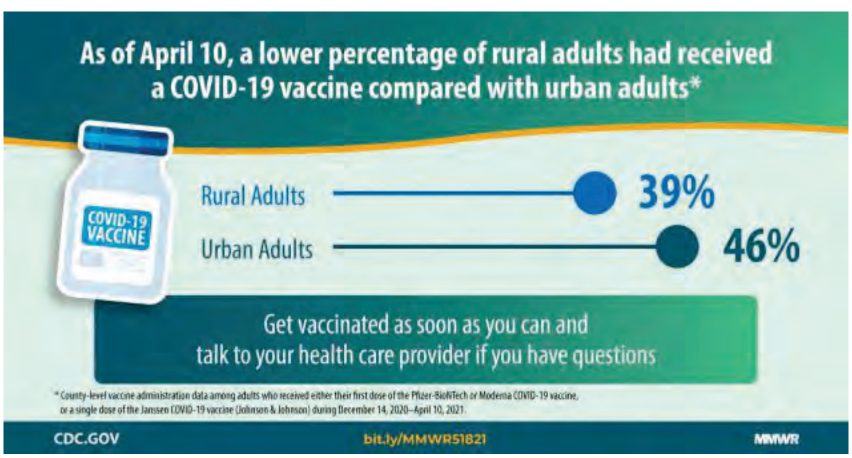
Figure 2

Table

References

Related Materials

PDF [181K]



Approximately 60 million persons in the United States live in rural counties, representing almost one fifth (19.3%) of the population.* In September 2020, COVID-19 incidence (cases per 100,000 population) in rural counties surpassed that in urban counties (*1*). Rural communities often have a higher proportion of residents who lack health insurance, live with comorbidities or disabilities, are aged ≥65 years, and have limited access to

health care facilities with intensive care capabilities, which placed these residents at increased risk for COVID-19–associated morbidity and mortality (*2*,*3*). To better understand COVID-19 vaccination disparities across the urban-rural continuum, CDC analyzed county-level vaccine administration data among adults aged ≥18 years who received their first dose of either the Pfizer-BioNTech or Moderna COVID-19 vaccine, or a single dose of the Janssen COVID-19 vaccine (Johnson & Johnson) during December 14, 2020–April 10, 2021 in 50 U.S. jurisdictions (49 states and the District of Columbia [DC]). Adult COVID-19 vaccination coverage was lower in rural counties (38.9%) than in urban counties (45.7%) overall and among adults aged 18–64 years (29.1% rural, 37.7% urban), those aged ≥65 years (67.6% rural, 76.1% urban), women (41.7% rural, 48.4% urban), and men (35.3% rural, 41.9% urban). Vaccination coverage varied among jurisdictions: 36 jurisdictions had higher coverage in urban counties, five had higher coverage in rural counties, and five had similar coverage (i.e., within 1%) in urban and rural counties; in four jurisdictions with no rural counties, the urban-rural comparison could not be assessed. A larger proportion of persons in the most rural counties (14.6%) traveled for vaccination to nonadjacent counties (i.e., farther from their county of residence) compared with persons in the most urban counties (10.3%). As availability of COVID-19 vaccines expands, public health practitioners should continue collaborating with health care providers, pharmacies, employers, faith leaders, and other community partners to identify and address barriers to COVID-19 vaccination in rural areas (*2*).

Data on COVID-19 vaccine doses administered in the United States are reported to CDC by jurisdictions, pharmacies, and federal entities through immunization information systems (IISs),[†] the Vaccine Administration Management System,[§] or direct data submission.[¶] Adults aged ≥18 years with a valid county of residence in one of 49 states or DC who received their first COVID-19 vaccine dose** during December 14, 2020–April 10, 2021, and whose data were reported to CDC by April 15, 2021, were included in the analysis.[††] COVID-19 vaccine doses administered to persons living in Hawaii and in eight counties in California with <20,000 residents were excluded, because these states have data-sharing restrictions on county-level information reported to CDC. Vaccine doses administered to persons living in U.S. territories were also excluded because territorial jurisdictional divisions could not be mapped to urban-rural classifications at the county level.

First doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics (NCHS) urban-rural classification scheme. To further classify counties into two categories (urban versus rural), four of these six categories (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan) were combined into urban areas, and two (micropolitan and noncore) were combined into rural areas (*4*).

Vaccination coverage for adults aged ≥18 years was calculated overall and by age group (18–64 and ≥65 years), sex, jurisdiction, and two- and six-level urban-rural classification. Coverage by race and ethnicity was not calculated because information on race and ethnicity was missing for 40% of data. Population size was obtained by county, age group, and sex from the U.S. Census Bureau's 2019 Population Estimates Program (*5*). Because only the first dose of a 2-dose vaccination series or the only dose for a single-dose vaccine were analyzed, the total number of doses allowed per county was capped at the population size of the county.[§§] The percentage of persons who traveled outside their county of residence for vaccination was calculated at the national level and stratified by jurisdiction for both the two- and six-level urban-rural classifications. Tests for statistical significance were not conducted because the data represent the U.S. population (minus Hawaii and eight counties in California) and were not based on population samples.

First-dose COVID-19 vaccination coverage was lower in rural than in urban counties for adults overall (38.9% rural, 45.7% urban) (Table); for adults aged 18–64 years (29.1% rural, 37.7% urban) and for those aged ≥65 years (67.6% rural, 76.1% urban); for women (41.7% rural, 48.4% urban); and for men (35.3% rural, 41.9% urban). Among jurisdictions, coverage varied by urban-rural classification; in 36 (72%) jurisdictions, coverage was higher in urban counties, in five (10%) coverage was higher in rural counties, and in five (10%) coverage was similar (i.e., within 1%) in both urban and rural counties. Vaccination coverage by urban-rural classification could not be calculated for four jurisdictions that had no rural counties.

Overall, 67.1% of vaccinated persons were vaccinated in their county of residence and 98.3% in their state of residence. The proportion of persons who traveled outside their county of residence for vaccination varied by jurisdiction, based on the two-level urban-rural classification (Figure 1). Analysis using the six-level urban-rural classification found that a larger proportion of persons in large fringe metropolitan counties (i.e., suburban areas) and noncore counties (i.e., the most rural areas) traveled to nonadjacent counties (i.e., farther from their county of residence) for vaccination (13.9% and 14.6%, respectively) compared with persons in the most urban counties (10.3%) (Figure 2).

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Discussion

Among most U.S. jurisdictions analyzed, COVID-19 vaccination coverage was lower overall, among all age groups, and among men and women in rural compared with urban counties. Coverage among adults aged ≥65 years was higher than among younger adults in both rural and urban areas, likely because of vaccine eligibility criteria that prioritized older adults earlier in

the implementation of the vaccination program before vaccination was expanded to other age groups. Notably, vaccination coverage among women in both urban and rural areas was higher than that among men, possibly because of the increased likelihood of women seeking and using preventive care services (*6*), or women working in sectors that were prioritized for early vaccination, such as health care and education.[¶¶] Because residents of rural communities are at increased risk for severe COVID-19–associated illness and death (*2*,*3*), vaccination disparities between urban and rural areas might hinder efforts to reduce morbidity and mortality from COVID-19 nationally.

Travel outside county of residence was used as a marker of potential vaccine access difficulties that might be exacerbated in rural areas with sparse vaccination sites. Analysis using the six-level urban-rural classification identified that a higher percentage of persons in the most rural counties traveled to nonadjacent counties for vaccination compared with those in the most urban counties, which might be related to challenges with vaccine access and the dearth of pharmacies in some rural areas (*7*). In addition, more persons in suburban (i.e., large fringe metropolitan) areas traveled outside their county of residence for vaccination; the reasons for this are unclear.

Although vaccination coverage was higher in urban counties compared with that in rural counties in most jurisdictions, five jurisdictions had similar vaccination rates between urban and rural counties and in another five, the rate in rural counties surpassed that of urban counties. Jurisdictional characteristics reported in news media that might have contributed to increased vaccination coverage in rural areas included implementing tailored approaches based on local needs, partnering with local community-based organizations and faith leaders, and engaging with underserved populations directly and through partners.[***,†††] Local jurisdictions are collaborating with CDC to improve access to COVID-19 vaccines in rural areas by identifying and addressing barriers to vaccination. CDC is also using multiple channels to distribute vaccines, such as federal partners (e.g., the Indian Health Service and the Health Resources and Services Administration) and the Federal Retail Pharmacy program.[§§§]

Vaccine hesitancy in rural areas is a major barrier that public health practitioners, health care providers, and local partners need to address to achieve vaccination equity. In March 2021, a poll by the Kaiser Family Foundation found that vaccine hesitancy was highest in rural communities, with 21% of rural residents stating that they would “definitely not” get a vaccine compared with 10% of urban residents. Among the rural respondents, 45% of younger adults (aged 18–64 years) stated that they would “definitely not” get a vaccine compared with 8% of older adults (aged 60–69 years) (*8*). Rural residents who reported that they would “definitely not” get a vaccine were more likely to report not having a college degree and earning <$40,000 per year (*8*). Notably, 86% of rural residents report they trust their own health care providers for information on COVID-19 vaccines, which highlights the importance of public health practitioners working with established outpatient health care systems in rural areas (*9*). Through its Vaccinate with Confidence initiative, CDC continues to support rural jurisdictions and local partners in their efforts to improve access to, and bolster trust and confidence in, COVID-19 vaccines.[¶¶¶]

The findings in this report are subject to at least five limitations. First, vaccination coverage is not representative of the entire United States, because county of residence was missing for 9.2% of persons.**** Second, each jurisdiction prioritized population subgroups for vaccination differently, which might have also contributed to vaccination coverage differences between urban and rural populations. Third, COVID-19 vaccine supply changed substantially during the observed time period, and persons may have been willing to travel farther for vaccination at the beginning of this time period when vaccine supplies were low, compared with later time periods. Fourth, race and ethnicity were unknown for approximately 40% of persons with available county information; therefore, vaccination coverage could not be calculated on the basis of race and ethnicity. Improved data completeness is critical to measure and address racial and ethnic disparities in vaccination coverage. Finally, the NCHS urban-rural classification was developed in 2013, and counties that were classified as rural in 2013 might not be classified as rural during 2020–2021.

Disparities in COVID-19 vaccination between urban and rural communities can hinder progress toward ending the pandemic. Public health practitioners should continue collaborating with health care providers, pharmacies, community-based organizations, faith leaders, and local employers[††††] to address vaccine hesitancy and ensure equitable vaccine access and distribution, particularly in rural areas (*10*). These focused, multipartner efforts can help increase nationwide vaccination coverage and reduce morbidity and mortality from COVID-19.

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* https://www.census.gov/library/stories/2017/08/rural-america.html

† IISs are confidential, computerized, population-based systems that collect and consolidate vaccination data from providers in 64 jurisdictions nationwide and can be used to track administered vaccines and measure vaccination coverage. The 64 IIS jurisdictions comprise the 50 U.S. states, five U.S. territories (American Samoa, Guam, Northern Mariana Islands, Puerto Rico, and U.S. Virgin Islands), three freely associated states (Marshall Islands, Micronesia, and Palau), and six local jurisdictions (Chicago, Illinois; Houston, Texas; San Antonio, Texas; Philadelphia, Pennsylvania; New York, New York; and Washington, DC).

§ https://www.cdc.gov/vaccines/covid-19/reporting/vams/program-information.html

¶ https://www.cdc.gov/vaccines/covid-19/reporting/overview/IT-systems.html

** First dose of COVID-19 vaccine is defined either as the first of 2 doses for the Pfizer-BioNTech or Moderna vaccines, or a single dose for the Janssen (Johnson and Johnson) vaccine.

†† Providers are required to document vaccination in their medical records within 24 hours of administration and submit this documentation to their jurisdiction's immunization information systems within 72 hours of administration. 5 days of observation were included to account for any delays in reporting and transmission of records to CDC.

§§ For statistical analysis, the number of doses allowed per county was capped at population size minus one for a maximum vaccination coverage of 100%.

¶¶ https://khn.org/news/article/gender-vaccine-gap-more-women-than-men-vaccinated-against-covid/

*** https://www.cnn.com/2021/03/04/health/gila-county-arizona-vaccine-trnd/index.html

††† https://www.cnn.com/2021/03/09/us/alaska-covid-19-vaccine-success-trnd/index.html

§§§ https://www.cdc.gov/vaccines/covid-19/retail-pharmacy-program/index.html

¶¶¶ https://www.cdc.gov/vaccines/covid-19/vaccinate-with-confidence/strategy.html

**** Hawaii and eight California counties were excluded from analysis. More than 20% of persons receiving the first dose of a COVID-19 vaccine who live in Georgia, South Dakota, and West Virginia did not have data available for county of residence.

†††† https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/essentialworker/workplace-vaccination-program.html

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TABLE. Vaccination coverage among adults aged ≥18 years who received their first dose of COVID-19 vacci age group, and urban-rural classification† — United States,§ December 14, 2020–April 10, 2021

	No. (%) vaccinated						
		Six-level urban-rural classification					
Jurisdiction	Overall	Large central metropolitan	Large fringe metropolitan¶	Medium metropolitan	Small metropolitan	Micropolitan	Noncor
United States	**113,554,259 (44.7)**	**37,075,718 (47.1)**	**29,206,614 (45.8)**	**23,861,372 (45.4)**	**9,505,176 (40.9)**	**8,368,195 (39.7)**	**5,537,1 (37.8**
Alabama	**1,294,410 (33.9)**	221,812 (43.6)	99,898 (26.1)	366,648 (36.1)	336,235 (33.0)	124,904 (30.5)	144,91 (30.4
Alaska	**273,888 (49.7)**	—**	—**	148,209 (49.6)	31,389 (42.5)	22,787 (63.1)	71,50 (50.0
Arizona	**2,514,666 (44.6)**	1,444,473 (42.1)	137,650 (38.2)	442,370 (53.2)	333,991 (44.6)	109,132 (58.1)	47,05 (61.1
Arkansas	**838,457 (36.2)**	—**	10,405 (29.7)	432,025 (38.7)	96,973 (33.2)	149,145 (34.1)	149,9((34.3
California	**15,349,193 (50.3)**	10,168,806 (51.7)	1,986,161 (49.5)	2,543,570 (47.4)	385,248 (42.3)	200,457 (44.1)	64,95 (45.4
Colorado	**2,177,824 (48.4)**	301,043 (51.1)	838,482 (48.6)	649,740 (47.7)	106,506 (42.2)	164,065 (51.3)	117,98 (47.0
Connecticut	**1,565,628 (55.2)**	390,071 (55.3)	147,437 (56.9)	945,420 (54.8)	—**	82,700 (55.9)	—**
Delaware	**376,448 (48.9)**	—**	215,689 (49.1)	106,497 (55.7)	54,262 (38.9)	—**	—**
District of Columbia	**272,747 (47.2)**	272,747 (47.2)	—**	—**	—**	—**	—**

Jurisdiction	No. (%) vaccinated						
	Overall	Six-level urban-rural classification					
		Large central metropolitan	Large fringe metropolitan¶	Medium metropolitan	Small metropolitan	Micropolitan	Noncor
Florida	**7,558,301 (43.8)**	2,612,865 (43.8)	2,098,598 (43.9)	2,181,338 (44.4)	487,184 (48.1)	98,684 (33.7)	79,63 (28.2
Georgia	**1,570,189 (19.4)**	188,126 (22.5)	725,542 (19.4)	248,864 (26.8)	226,829 (18.7)	115,309 (15.0)	65,51 (10.3
Idaho	**545,857 (40.8)**	—**	—**	250,086 (44.3)	135,313 (39.9)	120,446 (37.3)	40,01 (35.9
Illinois	**4,798,337 (48.7)**	2,024,718 (50.2)	1,573,694 (50.0)	339,073 (48.5)	381,873 (46.1)	291,296 (43.1)	187,68 (40.4
Indiana	**2,057,161 (39.8)**	263,355 (36.2)	727,655 (43.9)	319,160 (42.6)	342,196 (37.5)	281,902 (36.6)	122,89 (35.2
Iowa	**1,187,572 (48.9)**	—**	—**	461,103 (49.4)	267,887 (51.4)	174,447 (46.2)	284,13 (47.6
Kansas	**1,041,465 (47.1)**	—**	367,647 (54.6)	208,267 (43.0)	179,347 (49.3)	165,309 (41.2)	120,89 (41.5
Kentucky	**1,523,875 (44.0)**	313,875 (52.5)	230,936 (43.6)	286,818 (50.6)	136,493 (39.4)	266,331 (39.9)	289,42 (38.2
Louisiana	**1,343,593 (37.7)**	165,679 (53.0)	308,584 (45.6)	484,513 (36.2)	217,680 (32.7)	88,773 (29.9)	78,36 (29.0
Maine	**575,911 (52.6)**	—**	—**	244,914 (55.7)	101,952 (48.6)	49,521 (50.0)	179,52 (51.7
Maryland	**2,300,883 (48.8)**	191,933 (40.5)	1,875,332 (50.6)	111,818 (42.4)	62,256 (43.0)	29,755 (53.5)	29,78 (45.4
Massachusetts	**2,611,958 (47.1)**	306,989 (45.7)	1,707,107 (51.1)	518,678 (44.6)	49,567 (17.4)	29,535 (40.8)	82 (0.9
Michigan	**3,414,578 (43.5)**	768,690 (41.8)	1,051,335 (44.6)	579,511 (44.3)	385,356 (42.9)	391,849 (43.4)	237,83 (44.2
Minnesota	**2,121,068 (48.9)**	736,642 (52.2)	562,068 (43.8)	108,924 (57.5)	241,769 (49.4)	258,667 (50.1)	212,99 (47.7
Mississippi	**828,073 (36.4)**	—**	65,816 (32.7)	298,780 (39.9)	39,999 (34.9)	257,322 (36.0)	166,15 (33.4
Missouri	**1,843,060 (38.7)**	320,345 (40.9)	800,596 (43.5)	137,447 (35.9)	213,023 (38.0)	174,846 (31.3)	196,80 (30.6
Montana	**372,927 (44.4)**	—**	—**	—**	139,699 (47.5)	109,748 (41.4)	123,48 (43.9

	No. (%) vaccinated						
		Six-level urban-rural classification					
Jurisdiction	Overall	Large central metropolitan	Large fringe metropolitan¶	Medium metropolitan	Small metropolitan	Micropolitan	Noncor
Nebraska	**718,993 (49.3)**	—**	—**	450,638 (51.6)	40,185 (49.7)	112,525 (45.6)	115,64 (45.1
Nevada	**1,015,950 (42.6)**	739,037 (42.3)	—**	179,391 (47.9)	21,360 (47.9)	67,238 (34.2)	8,924 (34.5
New Hampshire	**605,093 (54.8)**	—**	204,277 (57.1)	158,455 (47.6)	—**	214,430 (57.5)	27,93 (67.4
New Jersey	**3,516,994 (50.7)**	728,029 (46.3)	2,408,516 (52.4)	287,894 (49.4)	92,555 (48.7)	—**	—**
New Mexico	**943,664 (58.2)**	—**	—**	411,876 (57.3)	247,917 (65.1)	245,120 (54.6)	38,75 (53.0
New York	**7,449,653 (48.3)**	3,646,082 (45.9)	2,201,835 (51.7)	759,849 (52.3)	342,276 (50.5)	366,736 (46.9)	132,87 (42.5
North Carolina	**3,497,654 (42.7)**	807,462 (47.5)	384,965 (35.9)	1,326,943 (45.4)	302,213 (41.4)	485,062 (38.7)	191,00 (37.9
North Dakota	**266,915 (45.9)**	—**	—**	—**	148,378 (49.9)	51,760 (37.9)	66,77 (45.1
Ohio	**3,980,433 (43.7)**	1,225,497 (46.7)	876,242 (45.7)	1,053,437 (44.6)	146,003 (37.9)	558,642 (37.7)	120,61 (35.3
Oklahoma	**1,311,507 (43.6)**	316,961 (53.3)	195,507 (41.6)	361,732 (43.9)	40,249 (41.6)	240,550 (39.6)	156,50 (38.1
Oregon	**1,494,454 (44.6)**	332,259 (50.1)	393,659 (42.7)	286,399 (44.6)	247,465 (42.4)	194,569 (42.4)	40,10 (48.9
Pennsylvania	**4,817,265 (47.4)**	1,098,792 (49.2)	1,556,236 (52.9)	1,328,061 (46.2)	382,538 (40.3)	327,898 (38.9)	123,74 (38.0
Rhode Island	**407,784 (47.7)**	229,134 (45.1)	178,650 (51.5)	—**	—**	—**	—**
South Carolina	**1,575,298 (39.0)**	—**	105,409 (33.4)	1,071,517 (39.5)	182,137 (43.3)	132,651 (37.6)	83,58 (35.7
South Dakota	**247,945 (37.1)**	—**	—**	—**	128,452 (39.1)	64,444 (35.7)	55,04 (34.7
Tennessee	**2,032,692 (38.2)**	533,687 (42.5)	383,619 (36.9)	559,029 (41.0)	168,327 (36.7)	223,523 (32.6)	164,50 (31.9
Texas	**9,325,215 (43.2)**	4,562,747 (44.5)	1,848,021 (43.2)	1,575,372 (47.3)	502,046 (36.1)	458,287 (36.9)	378,74 (34.2

Jurisdiction	No. (%) vaccinated						
	Overall	Six-level urban-rural classification					
		Large central metropolitan	Large fringe metropolitan¶	Medium metropolitan	Small metropolitan	Micropolitan	Noncor
Utah	**1,039,555 (45.7)**	423,864 (49.8)	19,552 (39.9)	390,166 (42.8)	98,050 (44.2)	63,274 (47.2)	44,64 (41.9
Vermont	**269,382 (52.8)**	—**	—**	—**	93,365 (51.9)	110,027 (55.4)	65,99 (50.1
Virginia	**3,162,645 (47.4)**	463,230 (43.6)	1,799,645 (50.0)	244,719 (45.6)	302,185 (47.0)	86,015 (41.3)	266,85 (42.5
Washington	**2,745,505 (46.1)**	918,867 (51.0)	736,446 (42.9)	478,192 (42.9)	342,357 (48.2)	201,142 (42.3)	68,50 (51.2
West Virginia	**325,762 (22.7)**	—**	11,485 (25.8)	58,693 (22.8)	139,026 (23.8)	53,402 (22.7)	63,15 (20.2
Wisconsin	**2,267,575 (49.8)**	357,901 (49.7)	371,918 (51.0)	465,236 (57.3)	528,622 (48.0)	275,088 (44.4)	268,81 (47.0
Wyoming	**178,257 (40.1)**	—**	—**	—**	56,443 (41.1)	78,882 (42.7)	42,93 (34.9
Demographic characteristics							
Sex							
Male	**50,684,095 (41.0)**	16,606,553 (43.6)	12,926,239 (41.8)	10,606,151 (41.5)	4,266,165 (37.4)	3,756,557 (35.9)	2,522,4 (34.4
Female	**61,803,696 (47.4)**	20,118,007 (49.6)	16,023,200 (48.8)	13,032,454 (48.2)	5,149,771 (43.5)	4,519,824 (42.5)	2,960,4 (40.5
Age group, yrs							
18–64	**73,245,975 (36.6)**	25,903,354 (40.3)	18,997,421 (37.6)	14,910,642 (36.4)	5,681,032 (31.8)	4,798,499 (30.0)	2,955,0 (27.7
≥65	**40,147,289 (74.7)**	11,035,258 (76.4)	10,205,186 (76.9)	8,949,648 (77.3)	3,812,281 (70.8)	3,566,401 (69.8)	2,578,5 (64.7

* First dose of COVID-19 vaccine is defined either as the first of 2 doses for the Pfizer-BioNTech or Moderna vaccines, or a single dose for the Janssen (Johnson & Johnson) vaccine.

† First doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics urban-rural classification scheme (https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf). To further classify counties into two categories (urban versus rural), four of these six categories were combined into urban areas (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan) and two were combined into rural areas (micropolitan and noncore).

§ Excludes doses with state of residence reported as Hawaii, a territory, an island, or a county of residence in California with population <20,000. Completeness of county data varied by jurisdiction. Three states (Georgia, South Dakota, and West

Virginia) had <80% completeness for county of residence data.

¶ Large fringe metropolitan refers to suburban areas.

** Jurisdiction does not have any counties at this level of urban-rural classification.

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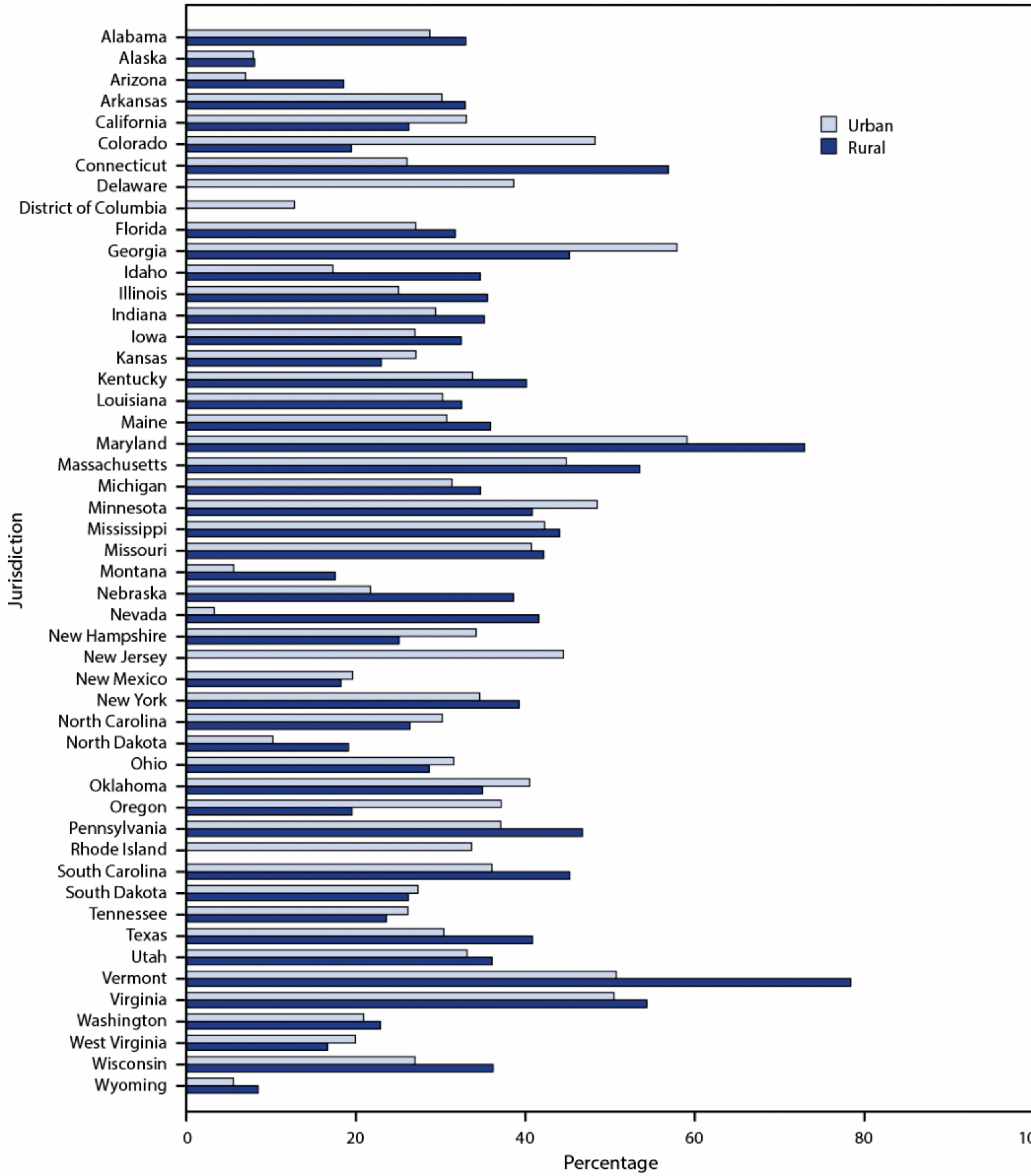
FIGURE 1. Percentage of vaccinated persons who traveled outside their county of residence* for their first dose of COVID-19 vaccine,† by jurisdiction and urban-rural classification§ — United States, December 14, 2020–April 10, 2021



* Excludes doses with state of residence reported as Hawaii, a territory, an island, or a county of residence in California with population <20,000. Completeness of county data varied by jurisdiction. Three states (Georgia, South Dakota, and West Virginia) had <80% completeness for county of residence data. Four jurisdictions (Delaware, New Jersey, Rhode Island, and District of Columbia) did not have rural counties.

† First dose of COVID-19 vaccine is defined either as the first of 2 doses for the Pfizer-BioNTech or Moderna vaccines, or a single dose for the Janssen (Johnson & Johnson) vaccine.

§ First doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics urban-rural classification scheme (https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf). To further classify counties into two categories (urban versus rural), four of these six categories were combined into urban areas (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan) and two were combined into rural areas (micropolitan and noncore).

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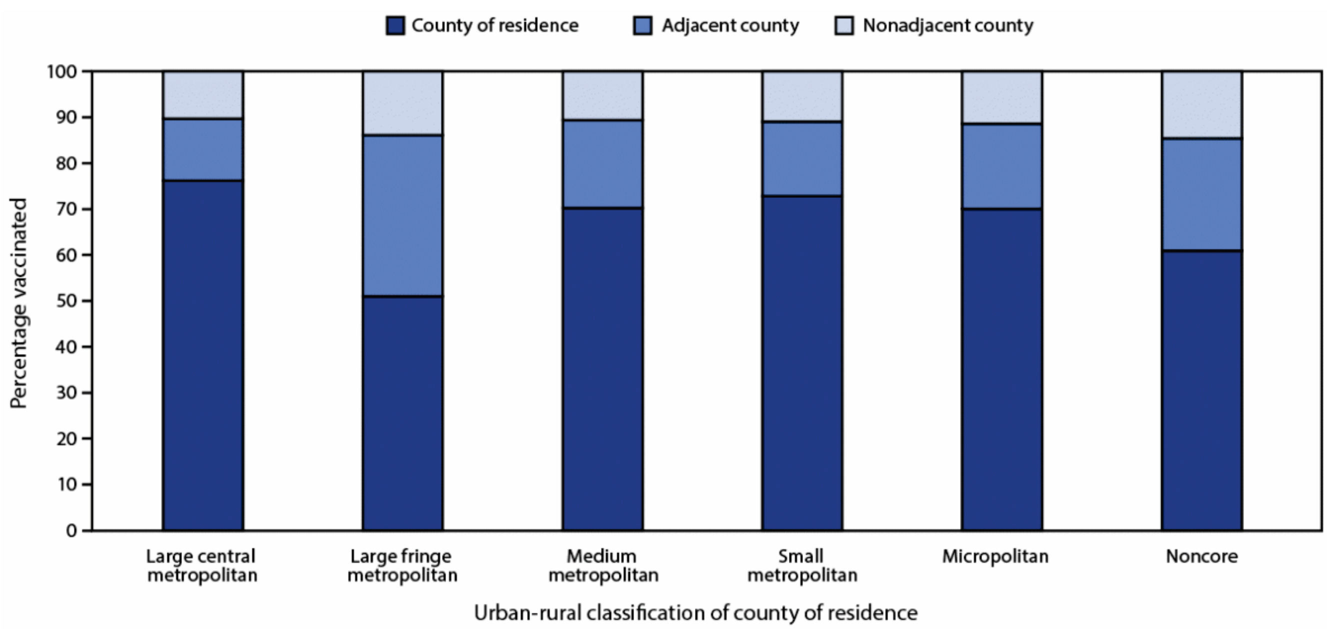
FIGURE 2. Location of receipt of first COVID-19 vaccine dose* among vaccinated persons, by urban-rural classification of county of residence†,§,¶ — United States, December 14, 2020–April 10, 2021



* First dose of COVID-19 vaccine is defined either as the first of 2 doses for the Pfizer-BioNTech or Moderna vaccines, or a single dose for the Janssen (Johnson & Johnson) vaccine.

† Excludes doses with state of residence reported as Hawaii, a territory, an island, or a county of residence in California with population <20,000. Completeness of county data varied by jurisdiction. Three states (Georgia, South Dakota, and West Virginia) had <80% completeness for county of residence data.

§ First doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics urban-rural classification scheme (https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf). To further classify counties into two categories (urban versus rural), four of these six categories were combined into urban areas (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan) and two were combined into rural areas (micropolitan and noncore).

¶ Large fringe metropolitan refers to suburban areas.

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OFFICE OF SCIENCE & DATA POLICY

ISSUE BRIEF

APRIL 2021

Disparities in COVID-19 Vaccination Rates across Racial and Ethnic Minority Groups in the United States

KEY POINTS

- As of March 3, 2021, 38 states and the District of Columbia reported race or ethnicity for individuals who have received at least one dose of the COVID-19 vaccine. Although nearly half of vaccinations have unknown race or ethnicity in national data, data completeness for states in this brief ranges from 67% to 99%.
- Across all reporting states, a lower proportion of the Black and Hispanic populations have been vaccinated compared to the non-Hispanic White population.
- The percentage of vaccinated people who are Black or Hispanic is lower than expected given the racial and ethnic demographics of healthcare workers, essential workers, and people over age 65.
- Vaccine accessibility issues, including challenges with vaccine scheduling, transportation and other concerns, likely contribute to lower vaccination rates in Black and Hispanic populations.

INTRODUCTION

The COVID-19 pandemic has exacerbated existing health disparities and has had a disproportionate impact on racial and ethnic minority groups in the United States.[1] In particular, Black, Hispanic, American Indian and Alaska Native, and Native Hawaiian or Pacific Islander populations have all experienced higher rates of infections, hospitalizations, and deaths due to COVID-19 relative to non-Hispanic White populations,[2,3] as well as higher rates of excess deaths during the pandemic.[4] Although disparities have not been evident for Asian populations in national data, disparities in infection, hospitalization, and death rates for Asian and Asian sub-

[1] In this brief, the term racial and ethnic minority group refers to Black, Hispanic, Asian, American Indian and Alaska Native, and Native Hawaiian or Pacific Islander populations in the U.S.

[2] Disparities in rates of COVID-19 infection, hospitalization, and death by race and ethnicity. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. November 10, 2020.

[3] Simmons A, Chappel A, Kolbe AR, Bush L, and Sommers BD. Health Disparities by Race and Ethnicity During the COVID-19 Pandemic: Current Evidence and Policy Approaches. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. March 16, 2021.

[4] Rossen LM, Branum AM, Ahmad FB, Sutton P, Anderson RN. Excess Deaths Associated with COVID-19, by Age and Race and Ethnicity — United States, January 26–October 3, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1522–1527. DOI: http://dx.doi.org/10.15585/mmwr.mm6942e2.

populations are evident in state or local data.[5,6] The COVID-19 vaccines that have been developed and received emergency use authorization (EUA) are highly safe and effective and as a result have the potential to reduce disparities in COVID-19 cases, hospitalizations, and deaths across racial and ethnic minority populations. Due to the disproportionate impact that COVID-19 has had on these populations, it is essential to ensure that the COVID-19 vaccine is distributed equitably across racial and ethnic minority populations.

The Advisory Committee on Immunization Practices (ACIP) recommendations for vaccine prioritization were developed and subsequently adopted by the Centers for Disease Control and Prevention (CDC) to ensure that those at highest risk of exposure and/or more severe illness were among the first to become eligible to be vaccinated.[7] Although ACIP recommendations do not explicitly address equity for racial or ethnic minority populations, these high-priority groups may also overlap with certain racial and ethnic groups based on their higher prevalence in the essential workforce or higher rates of certain comorbidities. Some states have developed specific plans to ensure equitable distribution of the vaccine to racial and ethnic minority populations.[8] Additionally, the CDC and Health Resources and Services Administration (HRSA) have launched a program to directly allocate vaccine doses to federally qualified health centers, with a focus on ensuring equity in vaccine distribution.[9]

Particular areas of focus to ensure equitable distribution to racial and ethnic minority populations have included combating vaccine hesitancy and ensuring fair and equal access to vaccination appointments. While COVID-19 vaccine hesitancy has decreased overall in recent months, rates of COVID-19 vaccine hesitancy are still higher for Black Americans than any other minority group,[10,11] in part due to historical as well as present-day medical malpractice and inequalities.[12,13] Vaccine accessibility issues range from the location of vaccination sites[14] and transportation to vaccination sites to the complex vaccine scheduling and registration process.[15] Disparities in vaccination rates due to accessibility issues have been particularly stark in cities where a disproportionate

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[5] Moore JT, Ricaldi JN, Rose CE, et al. Disparities in Incidence of COVID-19 Among Underrepresented Racial/Ethnic Groups in Counties Identified as Hotspots During June 5–18, 2020 — 22 States, February–June 2020. MMWR 2020;69:1122–1126.

[6] Marcello RK, Dolle J, Tariq A, Kaur S, Wong L, Curcio J et al. Disaggregating Asian Race Reveals COVID19 Disparities among Asian Americans at New York City's Public Hospital System. medRxiv. 2020. doi:10.1101/2020.11.23.20233155

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[14] NPR. Across the South, COVID-19 Vaccine Sites Missing from Black and Hispanic Neighborhoods. Accessed at https://www.npr.org/2021/02/05/962946721/across-the-south-covid-19-vaccine-sites-missing-from-black-and-hispanic-neighbor

[15] FiveThirtyEight. The reason Black Americans are getting vaccinated at a much slower rate is not because they're reluctant. Accessed at https://fivethirtyeight.com/features/why-fewer-black-americans-are-getting-the-covid-19-vaccine-no-its-not-hesitancy/

number of vaccines have been distributed to more affluent zip codes with lower minority populations.[16,17,18] This brief aims to summarize the existing state of COVID-19 vaccination data, identify where disparities are occurring, and explore factors that may influence disparities in vaccination rates for racial and ethnic minority groups.

METHODS

This brief uses two metrics to describe vaccinations by race and ethnicity. **Vaccine coverage describes the proportion of a given population that has received at least one dose of the COVID-19 vaccine**. For example, if a state has administered 10,000 vaccines to Black residents and there are 100,000 Black residents in the state, the vaccine coverage for the Black population would be 10% (10,000/100,000). Vaccine coverage accounts for the population size of each group and therefore can be used to compare the vaccination rates of different racial and ethnic groups. In order to evaluate whether equitable vaccine coverage has been achieved across all racial and ethnic groups, the vaccine coverage of racial and ethnic minority groups was compared to the non-Hispanic White population using a ratio (non-Hispanic White vaccine coverage divided by minority population vaccine coverage). The total population by race and ethnicity in each state was obtained from 2019 1-year American Community Survey (ACS) estimates. **The second metric used in this brief is the proportion of the vaccinated population that belongs to a given population**. For example, if a state has vaccinated 10,000 people, of which 1,000 are Black, then 10% of the vaccinated population are Black. This metric is population size dependent and therefore can be used to compare the demographics of vaccine recipients with the demographics of a population of interest (i.e., healthcare workers).

The number of vaccinated individuals in each state by race and ethnicity was obtained from state department of health websites on March 3, 2021. These data represent total vaccines administered as of between February 25, 2021 and March 3, 2021, depending on the frequency with which states update their publicly available data. At the time of data collection, no state was reporting vaccinations with the one-dose Johnson & Johnson vaccine; therefore, all data reported in this brief represent two-dose regimens with the Pfizer-BioNTech or Moderna vaccines. While the majority of states presented race or ethnicity data for individuals who had received at least one dose of the COVID-19 vaccine, a few states (Delaware, Illinois, Iowa, and Nevada) reported race or ethnicity for total administered doses. This means that people who have received both doses are double-counted in these four states. An additional four states (New Mexico, North Dakota, Vermont, and Wisconsin) reported vaccine coverage by race or ethnicity using the vaccine coverage metric described in the previous paragraph, but did not provide breakdowns of demographics by vaccines administered. These states are included in analysis of vaccine coverage, but omitted from analysis of share of vaccinations received.

For the purposes of comparing the racial and ethnic demographics of the vaccinated population to the racial and ethnic demographics of vaccine priority groups, three non-overlapping cohorts were identified: adults over the age of 65, healthcare workers under the age of 65, and non-healthcare essential workers under the age of 65. Race and ethnicity demographics for the non-institutionalized population over age 65 was obtained from the 2019 1-year ACS Public Use Microdata. Estimates of the population over age 65 do not include residents of

[16] The New York Times. New ZIP code data reflects disparities in N.Y.C.'s vaccination effort, officials say. Accessed at https://www.nytimes.com/2021/02/16/nyregion/nyc-covid-vaccine-zip-codes.html

[17] Los Angeles Times. New map shows deep inequities in L.A.'s COVID-19 vaccine rollout. Accessed at https://www.latimes.com/projects/la-covid-vaccine-racial-disparities-by-neighborhood-map/

[18] DCist. Black D.C. Residents Say They Want The COVID-19 Vaccine. But the Barriers to Access Are Many. Accessed at https://dcist.com/story/21/01/27/black-dc-residents-want-coronavirus-vaccine-but-lack-access/

long-term care facilities. However, vaccinations of long-term care residents represent a relatively small percentage of all vaccinations and are not expected to significantly skew the results of this analysis.

Estimates of race and ethnicity for healthcare workers were obtained from the Current Population Survey Annual Social and Economic Supplement (March 2020).[19] A respondent was considered to be a healthcare worker if the main job they held during the previous week fell into one of the following categories: offices of physicians, dentists, chiropractors, optometrists, or other health practitioners; outpatient care centers; home health care services; other health care services; general medical and surgical hospitals and specialty (except psychiatric and substance abuse) hospitals; psychiatric and substance use hospitals; nursing care facilities; and residential care facilities without nursing. These industries corresponded to Census codes 7970-8180, 8191, 8192, 8270, and 8290.[20] Only individuals under age 65 were included in these estimates of healthcare workers in order to prevent overlaps with the demographics for individuals over age 65.

Estimates of race and ethnicity for non-healthcare essential workers were also obtained from the Current Population Survey Annual Social and Economic Supplement (March 2020).[21] A respondent was considered to be a non-healthcare essential worker if the main job they held during the previous week fell into the essential worker industries and occupations outlined by the Cybersecurity and Infrastructure Security Agency (CISA),[22] excluding those captured by the healthcare worker codes listed above. These industries and occupations include frontline essential workers such as first responders, educators, and food and agriculture workers, as well as other essential workers defined in Phase 1b and Phase 1c of the ACIP recommended vaccine phases.[23] Only individuals under age 65 were included in estimates of essential workers in order to prevent overlaps with the demographics for individuals over age 65.

RESULTS

Vaccination rates by race and ethnicity

As of March 3, 2021, 38 states and the District of Columbia reported race for vaccinated individuals. Of these, 33 states also reported ethnicity. Although national data from CDC as of March 9, 2021 is missing race or ethnicity for approximately 46.8% of vaccinated individuals,[24] the completeness of demographic data from state departments of health is higher and reflects the between-state variation in data collection and reporting. Nearly all vaccinations have associated race or ethnicity data in North Carolina (99.5%), whereas only 61.7% of vaccinations have associated race or ethnicity data in Michigan (Appendix Figure 1). On average, states have associated race or ethnicity data for 83.5% of vaccinated people. Two states (Nevada and New York) provided race or ethnicity as a percentage of vaccinations with known race or ethnicity and did not provide the number of vaccinations with unknown race or ethnicity.

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[19] U.S. Census Bureau. Current Population Survey. Accessed at https://www.census.gov/programs-surveys/cps.html

[20] Current Population Survey: 2020 Annual Social and Economic (ASEC) Supplement. Appendix A – Industry Classification. Accessed at https://www2.census.gov/programs-surveys/cps/techdocs/cpsmar20.pdf

[21] U.S. Census Bureau. Current Population Survey. Accessed at https://www.census.gov/programs-surveys/cps.html

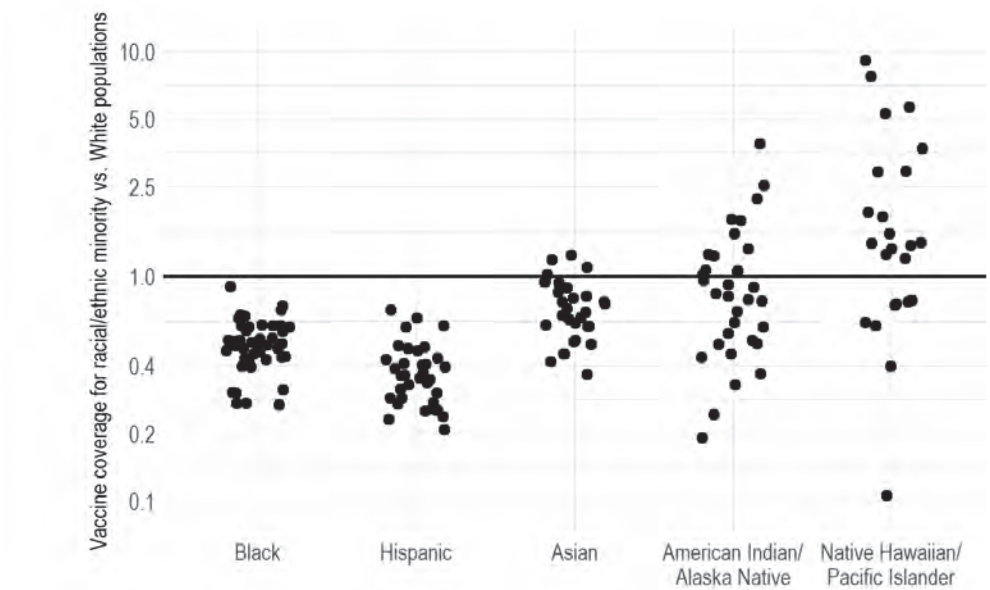
[22] CDC. Identify Essential Workers for Public Health Data Collection and Analysis. Accessed at https://www.cdc.gov/niosh/topics/coding/essentialworkers/default.html

[23] CDC. Interim List of Categories of Essential Workers Mapped to Standardized Industry Codes and Titles. https://www.cdc.gov/vaccines/covid-19/categories-essential-workers.html

[24] CDC. COVID Data Tracker: Demographic Characteristics of People Receiving COVID-19 Vaccinations in the United States. Accessed at https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic

Vaccine coverage of the Black and Hispanic populations was consistently lower than vaccine coverage of the non-Hispanic White population in each state (Figure 1). On average, vaccine coverage was approximately 2.1 and 2.9 times higher for the White population relative to the Black and Hispanic populations, respectively. Fewer states reported vaccination data for Asian, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander populations. Vaccine coverage for the Asian population tended to be lower than the non-Hispanic White population, but some states had near-equal vaccine coverage between Asian and White populations. Vaccine coverage for American Indian/Alaska Native and Native Hawaiian/Pacific Islander populations had larger variation, likely due to the smaller population sizes in many states (i.e., small numbers of vaccinations can result in large shifts in the coverage of the population). However, these data indicate that vaccine distribution has been more equitable between some groups than others. While disparities are evident in all reporting states for both the Black and Hispanic populations, some states achieved greater equity particularly for the American Indian/Alaska Native and Native Hawaiian/Pacific Islander populations. For the American Indian/Alaska Native population, these successes may be due in part to the targeted vaccine rollout strategy executed by the Indian Health Service.[25] This result highlights the importance of identifying and learning from successful approaches to achieve vaccine equity across vulnerable populations. However, due to the consistent disparities observed for vaccine coverage of the Black and Hispanic populations across all states, the remainder of the brief will focus on vaccination rates for Black and Hispanic populations.

Figure 1: State-level Vaccine Coverage of Racial and Ethnic Groups Relative to non-Hispanic Whites.



Notes: Vaccine coverage for racial and ethnic minority populations presented as a ratio of vaccine coverage for the minority population over the vaccine coverage for the non-Hispanic White population. Each point represents a single state. A value of 1 indicates equal vaccine coverage for the minority population and the non-Hispanic White population. Values greater than 1 indicate that a larger share of the minority population has been vaccinated compared to the non-Hispanic White population; values lower than 1 indicate that a larger share of the non-Hispanic White population has been vaccinated compared to the minority population. For states that reported data on ethnicity separately from race, the ratio was calculated as the coverage of the Hispanic population relative to the coverage of the non-Hispanic population. Eight states that combined data for Asian and Native Hawaiian/Pacific Islander are excluded in this figure.

[25] The Pew Charitable Trusts. In Hard-Hit Indian Country, Tribes Rapidly Roll Out Vaccines. Accessed at https://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2021/02/09/in-hard-hit-indian-country-tribes-rapidly-roll-out-vaccines

Due to the phased distribution of vaccines, vaccination demographics are not necessarily expected to align with the demographics of the state.[26] For example, the population over age 65 tends to be more White than the general population. However, healthcare and other essential workers include a large number of people in racial and ethnic minority groups. Nationally, 18% of healthcare workers and 15% of all essential workers are Black; 13% of healthcare workers and 21% of all essential workers are Hispanic.[27] Differences in occupational risk have been cited as one potential reason for the disproportionate impact of COVID-19 on racial and ethnic minority populations.[28] When combining the expected racial and ethnic demographics for people over 65, healthcare workers under age 65, and essential workers under age 65, Black and Hispanic people make up a lower than expected percentage of the total number of vaccinated people (Figure 2). When looking at each of these groups individually, the gap between share of vaccinated and share of population is smallest when looking only at adults over the age of 65 (Appendix Figure 2); however, vaccinations for Black and Hispanic populations still lag behind what would be expected if overall vaccination rates were driven primarily by the demographics of the 65+ population. The gaps are most significant for healthcare and other essential workers, where racial and ethnic minority groups make up a considerable fraction of the workforce in many states (Appendix Figures 3 and 4).

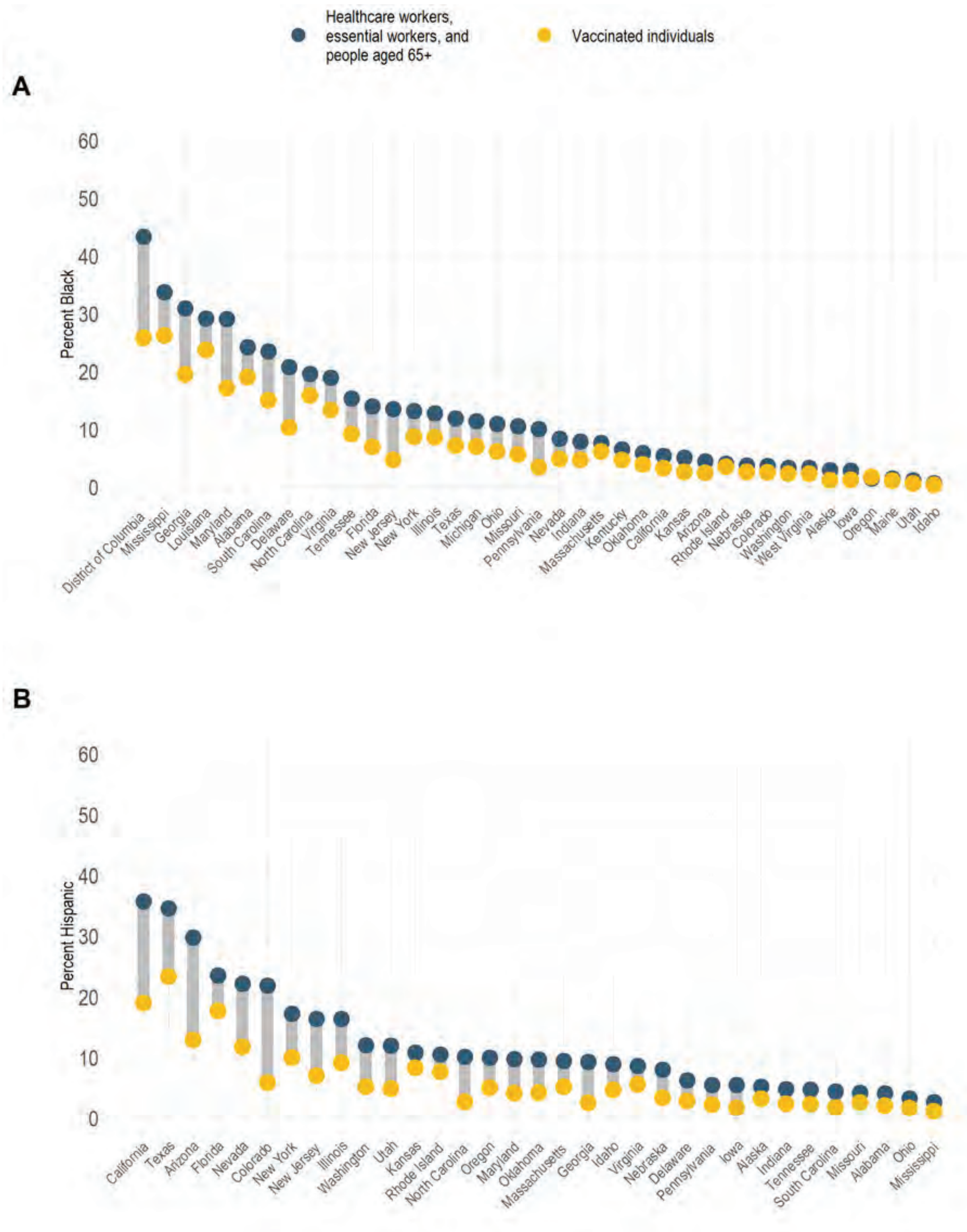
Together, these data indicate that Black and Hispanic populations consistently make up a disproportionately lower share of the vaccinated population than White or non-Hispanic populations, and Black and Hispanic populations are also being vaccinated at a lower rate than expected given their prevalence in priority vaccination groups.

[26] Painter EM, Ussery EN, Patel A, et al. Demographic Characteristics of Persons Vaccinated During the First Month of the COVID-19 Vaccination Program — United States, December 14, 2020–January 14, 2021. MMWR Morb Mortal Wkly Rep 2021;70:174–177. DOI: http://dx.doi.org/10.15585/mmwr.mm7005e1

[27] Economic Policy Institute. Who are essential workers? A comprehensive look at their wages, demographics, and unionization rates. Accessed at https://www.epi.org/blog/who-are-essential-workers-a-comprehensive-look-at-their-wages-demographics-and-unionization-rates/

[28] CDC. Health Equity Considerations and Racial and Ethnic Minority Groups. Accessed at https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html

Figure 2: Percent Black or Hispanic in Combined Priority Groups versus Vaccinated Population



Notes: Demographic data for healthcare workers, essential workers, and people over age 65 in each state were combined to estimate the percent of this combined population that is Black (A) or Hispanic (B) (represented by blue dot). This point represents the percentage of vaccinations that would be expected to be given to Black or Hispanic individuals if vaccines were administered equally across race and ethnicity among these three priority groups. The yellow dot represents the percentage of vaccinated individuals in a given state that are Black or Hispanic. States are ordered by the size of the Black or Hispanic population in the combined priority group. Not all states report vaccination rates for Hispanic populations; as a result, some states shown in (A) are not present in (B).

Role of vaccine hesitancy and accessibility in driving vaccination disparities

Two main explanations have emerged for disparities in vaccination rates among Black and Hispanic populations in the early rollout of the COVID-19 vaccine: vaccine hesitancy and accessibility. Vaccine hesitancy among racial and ethnic populations, particularly Black and Hispanic Americans, has been a significant concern for COVID-19 vaccines. Although COVID-19 vaccine enthusiasm has increased across racial and ethnic groups since the COVID-19 vaccine rollout began in December, the percent of Black adults who say they either have already been vaccinated or will as soon as possible is lower than White adults (41% vs. 61% in February 2021).[29] Black and Hispanic adults were more likely than White adults to say that they plan to "wait and see" how the COVID-19 vaccine works for other people.[30]

Data from the U.S. Census Bureau's Household Pulse Survey has shown decreases in vaccine hesitancy across racial and ethnic groups since the vaccine rollout began in December. When evaluating data from three relevant time points representing early February, late February, and early March, there was no consistent relationship observed between the coverage of the Black or Hispanic population and the rate of vaccine hesitancy in that population. Specifically, using data from the U.S. Census Bureau's Household Pulse Survey (Week 26: March 3 – March 15),[31] which represents hesitancy perspectives at the end of the data collection period, the percentage of Black or Hispanic respondents in a state who responded that they probably will not or definitely will not receive a COVID-19 vaccine was not significantly correlated with vaccine coverage of the Black or Hispanic population at the state level (Figure 3). Therefore, while vaccine hesitancy has frequently been cited as a driver of disparities in vaccination rates by race and ethnicity[32], attitudes toward the COVID-19 vaccines in early March 2021 cannot explain the observed variation in vaccine coverage for Black and Hispanic populations at the same time.

Compounding vaccine hesitancy for Black and Hispanic populations are the challenges associated with actually getting a vaccine. States have approached vaccine distribution in different ways, in terms of prioritization of who can be vaccinated, public information about COVID-19 vaccination, as well as where and when eligible residents can schedule vaccine appointments, being inconsistent and sometimes challenging to find.[33] One survey in January 2021 showed that Black and Hispanic adults were more likely than White adults to report that they did not have enough information about when and where they can receive a COVID-19 vaccine.[34] This information gap represents a first critical issue in vaccine accessibility for Black and Hispanic populations. Even when people have this information, however, scheduling vaccination appointments is another significant challenge. As of mid-February 2021, relatively few states operated a centralized system for residents to register for and schedule appointments to be vaccinated.[35] In many states, residents had to navigate multiple different online scheduling platforms to find a site with vaccine availability. Furthermore, relatively few states offered

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[29] Kaiser Family Foundation. KFF COVID-19 Vaccine Monitor: February 2021. Accessed at https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-february-2021/

[30] Kaiser Family Foundation. KFF COVID-19 Vaccine Monitor: February 2021. Accessed at https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-february-2021/

[31] U.S. Census Bureau. Week 26 Household Pulse Survey: March 3 – March 15. Accessed at https://www.census.gov/data/tables/2021/demo/hhp/hhp25.html

[32] Corbie-Smith G. Vaccine Hesitancy Is a Scapegoat for Structural Racism. JAMA Health Forum. Published online March 25, 2021. doi:10.1001/jamahealthforum.2021.0434

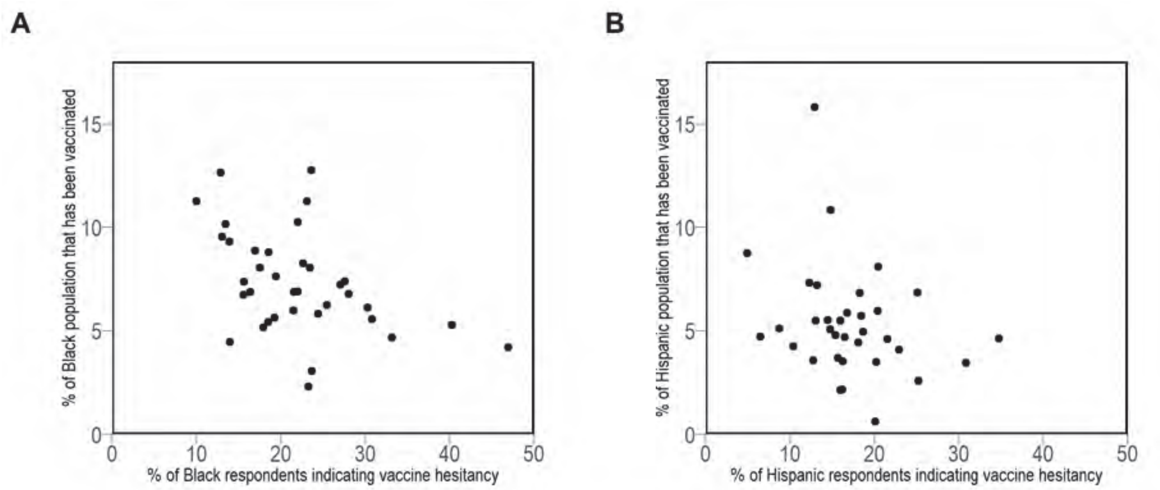
[33] Kolbe, A. Factors influencing variation between states in efficiency of COVID-19 vaccine administration. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. April 2021. Accessed at https://aspe.hhs.gov/pdf-report/covid-19-vaccine-administration

[34] Kaiser Family Foundation. KFF COVID-19 Vaccine Monitor: January 2021. Accessed at https://www.kff.org/coronavirus-covid-19/report/kff-covid-19-vaccine-monitor-january-2021/

[35] Kolbe, A. Factors influencing variation between states in efficiency of COVID-19 vaccine administration. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. April 2021. Accessed at https://aspe.hhs.gov/pdf-report/covid-19-vaccine-administration

phone assistance for vaccine scheduling. The complexity of the vaccine scheduling system is a significant barrier for people without computer or Internet access or those who are less comfortable with technology. Searching for and scheduling vaccination appointments favors those with time to dedicate to the effort and who have the flexibility to take time off work or travel long distances. Additionally, transportation to vaccination sites may present a barrier to getting vaccinated, particularly for older adults, people with disabilities, and low-income people. These challenges may disproportionately impact Black and Hispanic Americans, who are less likely to have a computer or Internet access in their home than non-Hispanic Whites or Asians,[36] and who make up disproportionate numbers of essential workers[37] that may not have the flexibility to take time off work to travel to vaccination sites.

Figure 3: Vaccine Coverage versus Vaccine Hesitancy for Black and Hispanic Populations



Notes: Vaccine coverage of the Black (A) and Hispanic (B) populations at the state level relative to vaccine hesitancy in those same populations at the state level as measured by the U.S. Census Bureau's Household Pulse Survey. Points represent individual states. Respondents were considered vaccine hesitant if they indicated that they probably will not or definitely will not receive a COVID-19 vaccine. Simple linear regression showed no significant correlation between vaccine coverage and vaccine hesitancy in either the Black or Hispanic population.

A recent ASPE issue brief highlighted the wide array of approaches states have taken to distribute their allotted vaccine doses.[38] As of mid-February 2021, the percentage of the population eligible to receive a vaccine in a given state varied from 20% to over 60%. States with the highest percentage of the population currently eligible to receive a vaccine had expanded eligibility to include adults with comorbidities. However, at the same time, no state had vaccinated over 21% of their population, which meant demand far exceeded supply, even assuming some vaccine eligible people were not actively seeking to be vaccinated. In some states, this led to significant technical issues with vaccine scheduling and registration.[39] Compounding this issue is the fact that in some of these states with expanded eligibility, residents of neighboring states with stricter vaccine eligibility

[36] The U.S. Census Bureau. The Digital Divide: Percentage of Households by Broadband Internet Subscription, Computer Type, Race and Hispanic Origin. Accessed at https://www.census.gov/library/visualizations/2017/comm/internet.html
[37] Rho, H., Brown, H., and Fremstad, S. (2020). A Basic Demographic Profile of Workers in Frontline Industries. Center for Economic and Policy Research, Washington, D.C. https://cepr.net/wp-content/uploads/2020/04/2020-04-Frontline-Workers.pdf
[38] Kolbe, A. Factors influencing variation between states in efficiency of COVID-19 vaccine administration. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. April 2021. Accessed at https://aspe.hhs.gov/pdf-report/covid-19-vaccine-administration
[39] Stat News. Vaccine registration technology is failing. Here's how the Biden administration could fix it. Accessed at https://www.statnews.com/2021/01/14/covid19-vaccines-technology-registration-websites/

requirements were crossing borders to receive a vaccine.[40] This level of demand exacerbates the accessibility issues discussed above, making navigating websites and scheduling platforms even more complicated and time-consuming.

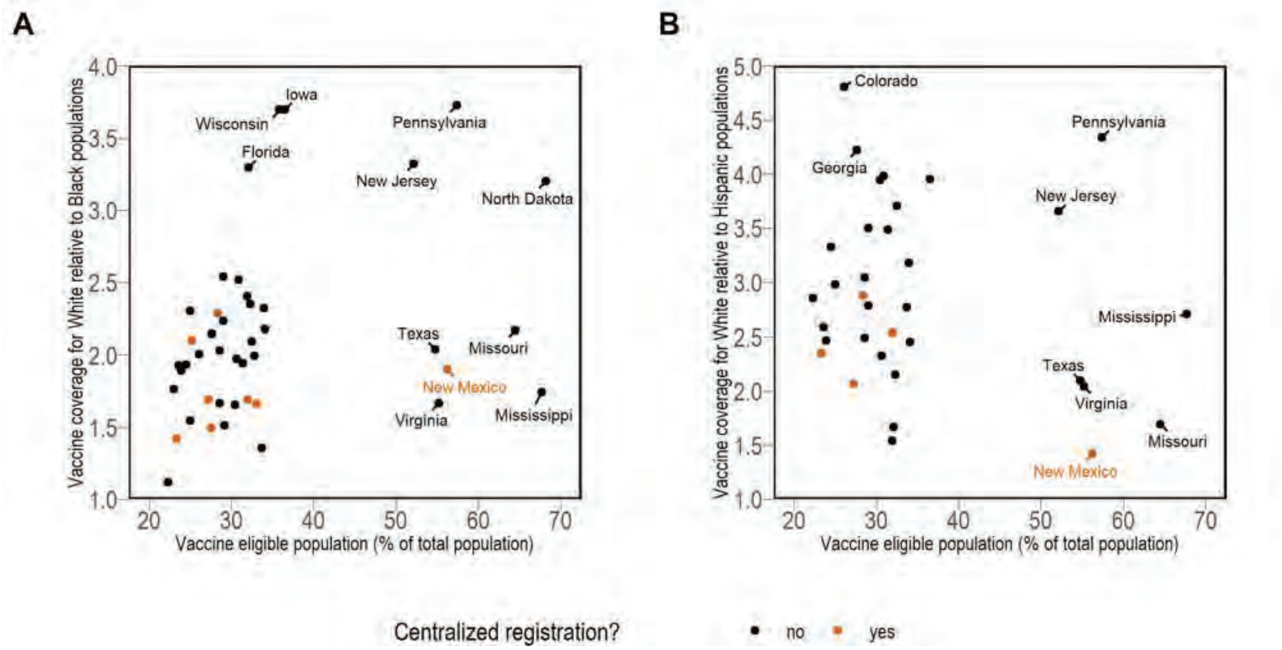
Across all states reporting race and ethnicity for COVID-19 vaccinations, there was a weak relationship between the size of the eligible population and disparities in terms of vaccine coverage rates for Black populations relative to non-Hispanic White populations (Figure 4A). In other words, states with a larger vaccine-eligible population tended to have larger disparities in vaccine coverage rates (slope = 0.017, R-squared = 0.11, p-value = 0.02). Even among states with more restrictive eligibility (i.e., <50% of population currently eligible), a greater vaccine eligible population was associated with greater disparities (slope = 0.079, R-squared = 0.29, p-value = 0.00095) This suggests that even relatively small differences in the vaccine eligible population may increase demand for vaccines and exacerbate disparities. Among the six states with the highest disparities for coverage of the Black population, all had higher than the median vaccine eligible populations (median across all states = 30.9), and three also had vaccine eligible populations >50% (Pennsylvania, New Jersey, and North Dakota). However, not all states with large vaccine eligible populations had large disparities: five states (Mississippi, Missouri, New Mexico, Texas, and Virginia) with >50% vaccine eligible populations had similar disparities for Black vaccination rates (range: 1.7 – 2.2) as states with lower vaccine eligible populations. This suggests that larger vaccine eligible populations may influence vaccination disparities in some states, but disparities in vaccination rates are likely influenced, at least in part, by factors other than the vaccine eligible population.

Interestingly, there was no statistically significant relationship between the size of the vaccine eligible population and disparities for Hispanic populations (Figure 4B). However, among states with >50% vaccine eligible population, states clustered in the same patterns as observed for disparities in Black populations (higher disparities in Pennsylvania and New Jersey; lower disparities in Mississippi, Missouri, New Mexico, Texas, and Virginia). This suggests that there may be state-specific policies or programs associated with higher or lower vaccine coverage across racial and ethnic populations. For example, states with centralized scheduling systems[41] tended to have lower disparities for both Black and Hispanic vaccination rates, which suggests that simplifying the vaccine scheduling system may result in more equitable outcomes. However, given the relatively small number of states that offered centralized registration at the time of data collection, additional research is necessary to evaluate the impact of centralized vaccine scheduling systems on achieving equity in vaccine distribution.

[40] The New York Times. Can't get a shot? Thousands of 'Vaccine Hunters' are crossing state borders to get theirs. Accessed at https://www.nytimes.com/2021/02/04/us/covid-vaccines-crossing-states.html

[41] States with centralized vaccine registration and scheduling systems were identified through state websites and media sources, as previously described (see Footnote 34). States that had a central system for state-run sites only (such as mass vaccination sites) were not considered to have centralized vaccine registration.

Figure 4: Relative Vaccine Coverage versus Vaccine Eligible Population



Notes: The ratio of vaccine coverage was calculated for non-Hispanic White populations relative to Black (A) and Hispanic (B) populations. The vaccine eligible population is calculated as a percent of the total population, and represents eligibility criteria as of mid-February 2021. Points represent individual states. A value of 1 for the ratio of vaccine coverage would indicate that equal shares of the White and Black/Hispanic populations have been vaccinated; a value of 2 indicates that Whites have been vaccinated at twice the rate as the minority group. Data points are colored based on whether the state had a centralized registration system for COVID-19 vaccines as of mid-February 2021. States with the largest disparities and the highest vaccine eligible population are labeled. Not all states report vaccination rates for Hispanic populations; as a result, some states shown in (A) are not present in (B).

DATA LIMITATIONS

Data completeness is a considerable limitation when interpreting racial and ethnic disparities among vaccinated individuals across the country. In general, vaccine coverage as a share of the population likely underestimates true vaccine coverage, due to large numbers of vaccinations reported without associated race or ethnicity in many states. Additionally, when comparing the percentage of vaccines that have been administered by race or ethnicity, the analysis in this brief inherently assumes that the vaccinations with no associated race or ethnicity information have a similar demographic composition as the vaccinations with associated race. However, if race and ethnicity reporting is lower for a specific minority group, this may result in an underestimation of the true numbers of vaccinations in these populations. Several states reported race and ethnicity for all doses administered, rather than individuals vaccinated; therefore, data from these states (Delaware, Illinois, Iowa, and Nevada) may not reflect the actual demographics of vaccinated individuals in the state and should be interpreted with caution.

Race and ethnicity data for long-term care facility residents are not readily available at the state level; therefore, this population is excluded from the analysis in this brief. Approximately 2 million residents of long-term care

facility residents have been vaccinated as of March 2021, making up around 3% of all vaccinated individuals.[42] By excluding this population, we may have over- or under-estimated the number of Black and Hispanic individuals that are expected to have received a vaccination based on membership in vaccination priority groups (Figure 2). However, given that this group represents a relatively small proportion of all vaccinations at this time and the size of the observed disparities, we expect that disparities would persist even with these additional data.

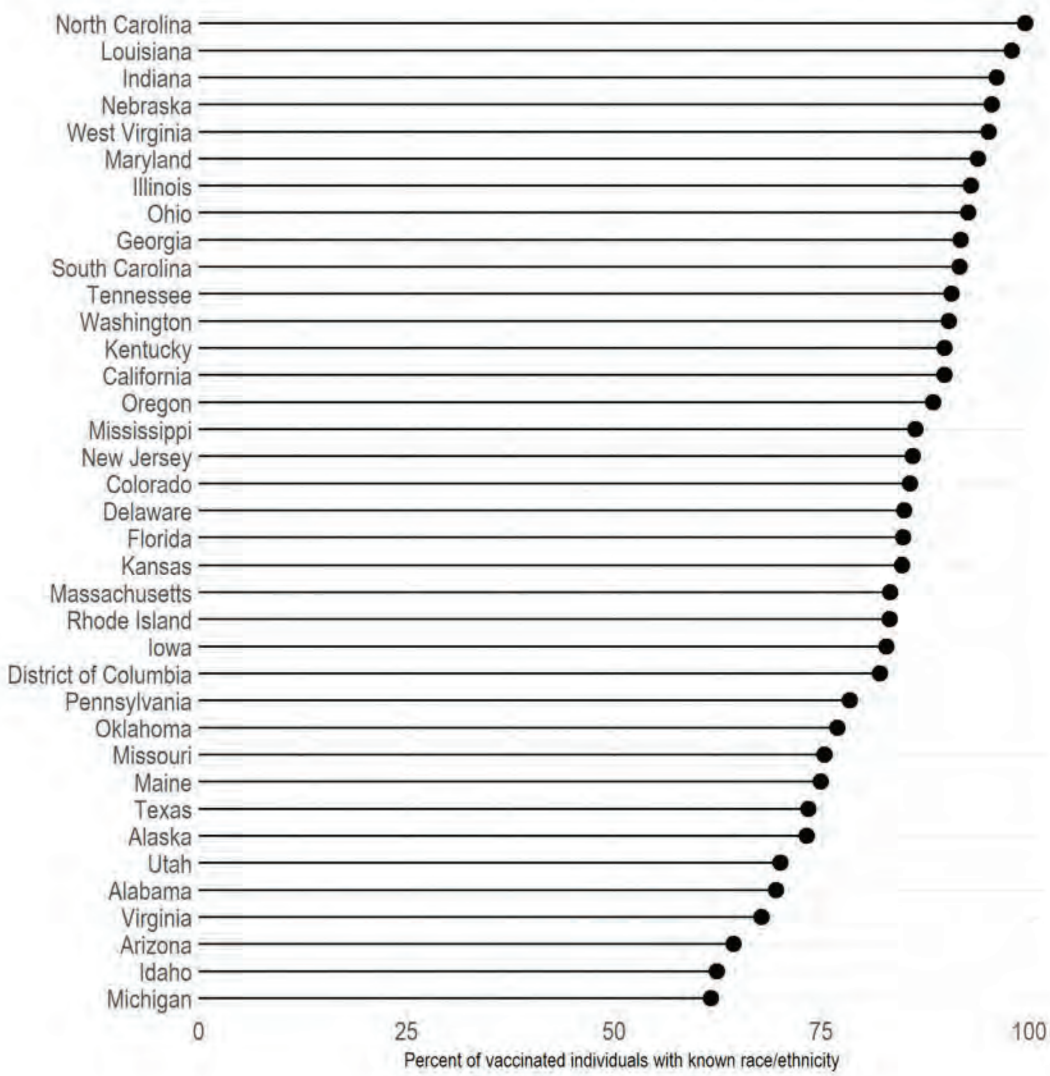
CONCLUSIONS

The majority of U.S. states are currently reporting at least some race or ethnicity data for COVID-19 vaccinations. Among those reporting states, Black and Hispanic populations have consistently received a lower share of the vaccine by population compared to White populations. When evaluating the membership of Black and Hispanic individuals in the vaccine priority groups of healthcare workers, essential workers, and adults over the age of 65, fewer vaccines have been administered to Black and Hispanic individuals than would be expected. These findings highlight the importance of continued tracking of vaccinations by race and ethnicity, and suggest that more work is necessary to ensure equitable distribution of the vaccine among racial and ethnic minority populations. Vaccine hesitancy does not appear to be a driver of disparities, but vaccine accessibility issues likely contribute to lower vaccination rates in Black and Hispanic populations. Identifying strategies to improve accessibility for vaccine registration and scheduling is critical, especially as vaccine supply continues to grow and more people will become eligible to receive a vaccination.

[42] CDC. COVID Data Tracker: Federal Pharmacy Partnership for Long-Term Care (LTC) Program.

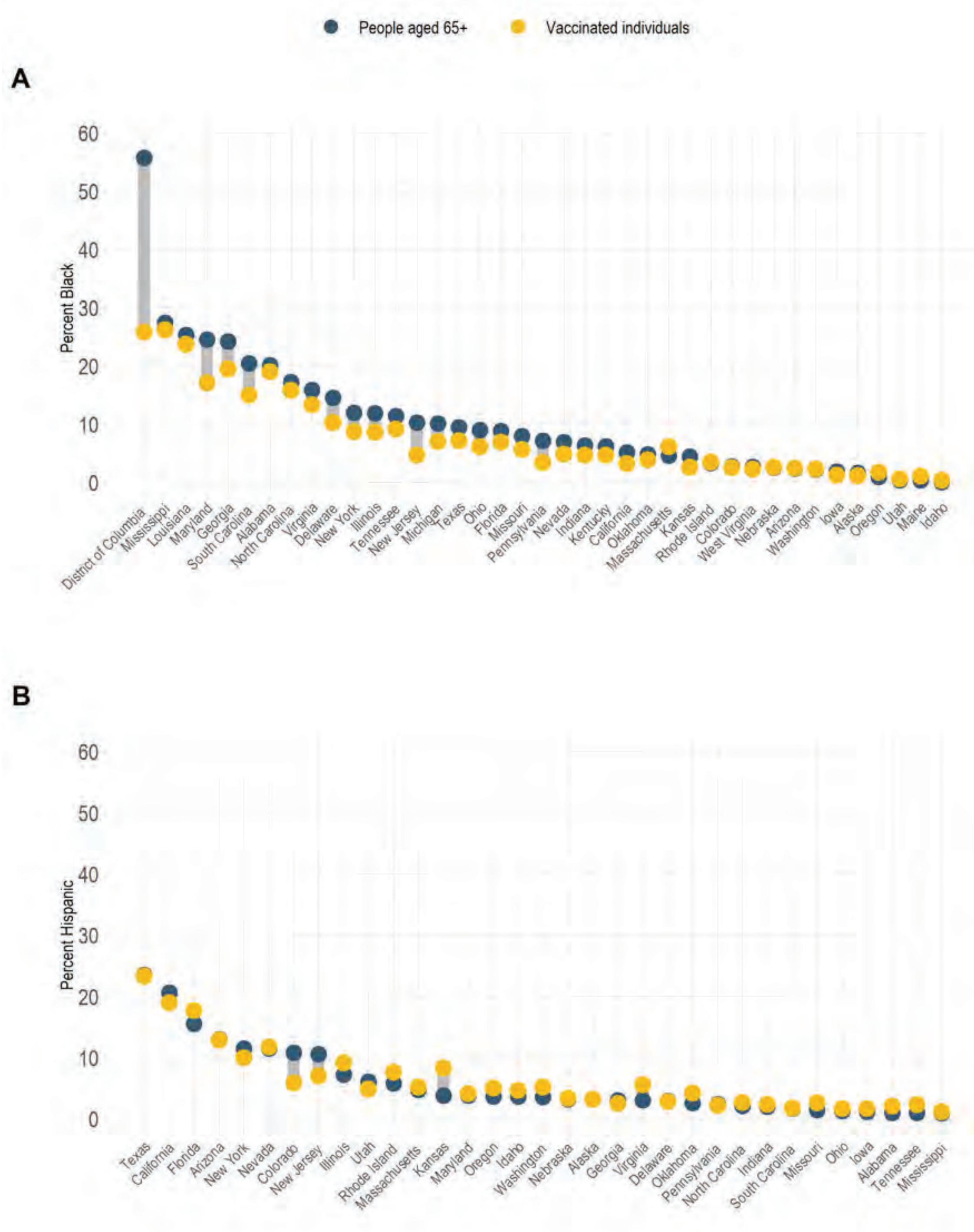
Appendix

Appendix Figure 1: Percent of Vaccinated Individuals with Known Race or Ethnicity, by State



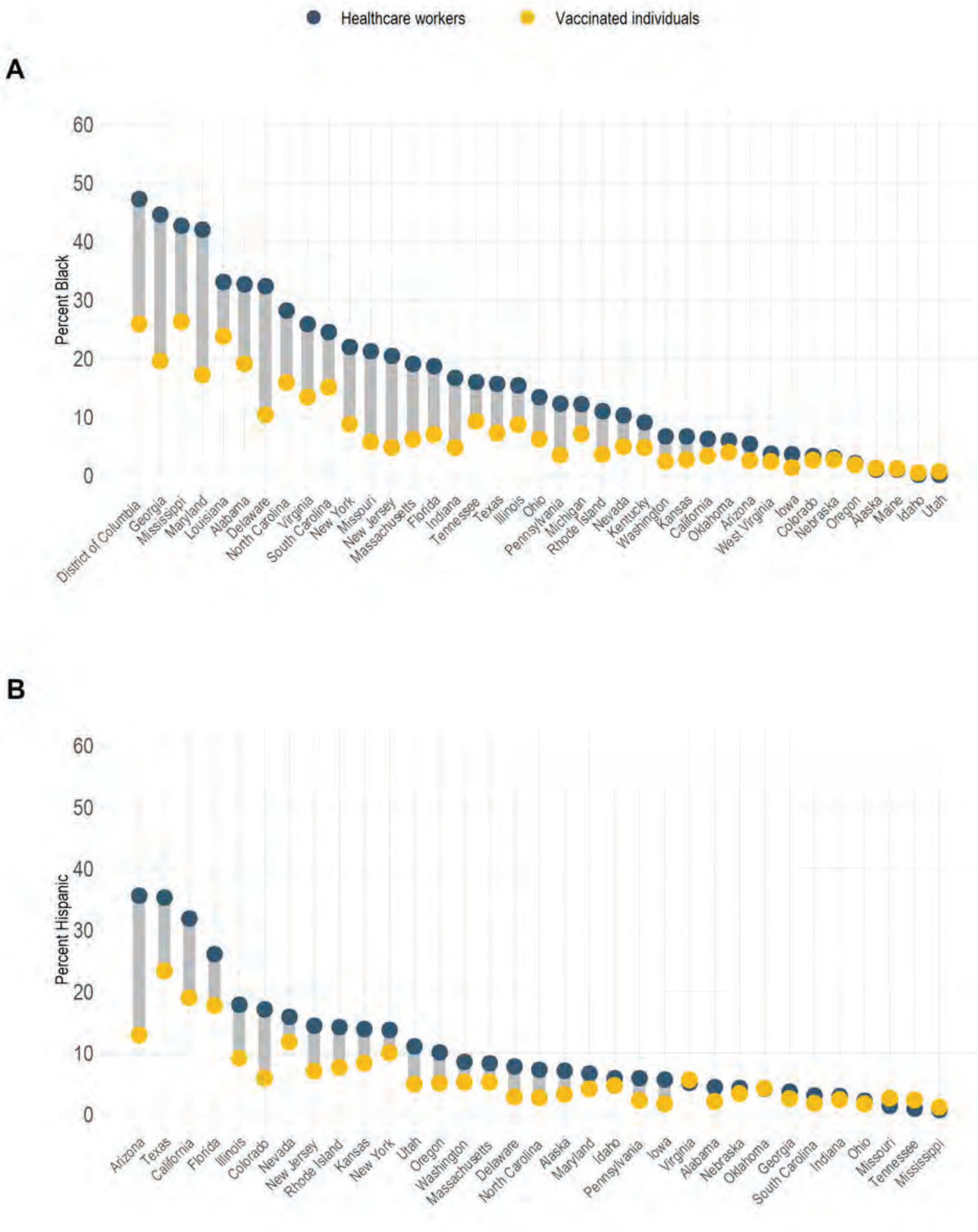
Notes: Nevada and New York do not report the percent of vaccinated individuals with unknown race or ethnicity and are excluded from this figure.

Appendix Figure 2: Percent Black or Hispanic in Age 65+ Population versus Vaccinated Population



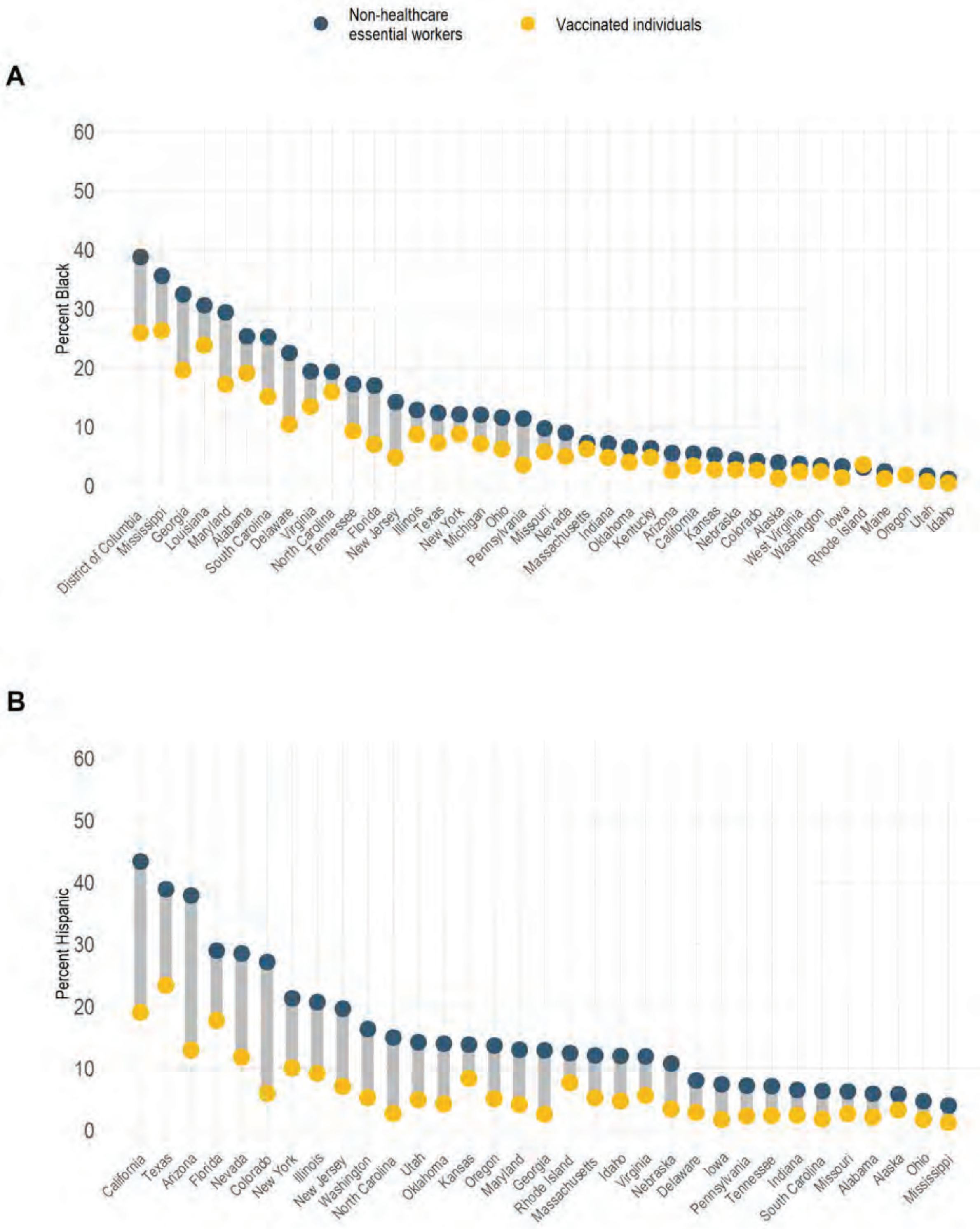
Notes: Blue dots represent the percent of the population over age 65 that is Black (A) or Hispanic (B). The yellow dot represents the percentage of vaccinated individuals in a given state that are Black or Hispanic. States are ordered by the size of the Black or Hispanic population in age 65+ population. Not all states report vaccination rates for Hispanic populations; as a result, some states shown in (A) are not present in (B).

Appendix Figure 3: Percent Black or Hispanic in Healthcare Workforce versus Vaccinated Population



Notes: Blue dots represent the percent of healthcare workforce (under age 65) that is Black (A) or Hispanic (B). The yellow dot represents the percentage of vaccinated individuals in a given state that are Black or Hispanic. States are ordered by the size of the Black or Hispanic population in the healthcare workforce. Not all states report vaccination rates for Hispanic populations; as a result, some states shown in (A) are not present in (B).

Appendix Figure 4: Percent Black or Hispanic in the Non-Healthcare Essential Workforce versus Vaccinated Population



Notes: Blue dots represent the percent of the non-healthcare essential workforce (under age 65) that is Black (A) or Hispanic (B). The yellow dot represents the percentage of vaccinated individuals in a given state that are Black or Hispanic. States are ordered by the size of the Black or Hispanic population in the non-healthcare essential workforce. Not all states report vaccination rates for Hispanic populations; as a result, some states shown in (A) are not present in (B).

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Do COVID-19 vaccines protect against the variants?

By Mayo Clinic Staff

October 7, 2021

What do I need to know about the delta variant?

Find out about the delta variant and how it spreads, and how a COVID-19 vaccine can protect you.

Video transcript

Key takeaways

In the U.S., the delta (B.1.617.2) variant is now the most common COVID-19 variant. It is nearly twice as contagious as earlier variants and might cause more severe illness. The greatest risk of transmission is among unvaccinated people. But people with vaccine breakthrough infections may also spread COVID-19 to others. However, it appears that vaccinated people spread COVID-19 for a shorter period than do unvaccinated people.

This variant also might reduce the effectiveness of some monoclonal antibody treatments and the antibodies generated by a COVID-19 vaccine.

The alpha, gamma and beta variants continue to be monitored but are spreading at much lower levels in the U.S. The mu variant is also being monitored.

While research suggests that COVID-19 vaccines are slightly less effective against the variants, the vaccines still appear to provide protection against severe COVID-19. For example:

- Early research from the U.K. suggests that, after full vaccination, the Pfizer-BioNTech COVID-19 vaccine is 88% effective at preventing symptomatic COVID-19 virus caused by the delta variant. The vaccine is 96% effective at preventing severe disease with the COVID-19 virus caused by the delta variant. The research also showed that the vaccine is 93% effective at preventing symptomatic COVID-19 virus caused by the alpha variant.
- Early research from Canada suggests that, after one dose, the Moderna COVID-19 vaccine is 72% effective at preventing symptomatic COVID-19 virus caused by the delta variant. One dose of the vaccine is also 96% effective at preventing severe disease with the COVID-19 virus caused by the delta variant.
- The Janssen/Johnson & Johnson COVID-19 vaccine is 85% effective at preventing severe disease with the COVID-19 virus caused by the delta variant, according to data released by Johnson & Johnson.

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Effect of Influenza Vaccination of Healthcare Personnel on Morbidity and Mortality Among Patients: Systematic Review and Grading of Evidence

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(See the Editorial Commentary by Griffin on pages 58–60.)

Background. Influenza vaccination of healthcare personnel (HCP) is recommended in >40 countries. However, there is controversy surrounding the evidence that HCP vaccination reduces morbidity and mortality among patients. Key factors for developing evidence-based recommendations include quality of evidence, balance of benefits and harms, and values and preferences.

Methods. We conducted a systematic review of randomized trials, cohort studies, and case-control studies published through June 2012 to evaluate the effect of HCP influenza vaccination on mortality, hospitalization, and influenza cases in patients of healthcare facilities. We pooled trial results using meta-analysis and assessed evidence quality using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results. We identified 4 cluster randomized trials and 4 observational studies conducted in long-term care or hospital settings. Pooled risk ratios across trials for all-cause mortality and influenza-like illness were 0.71 (95% confidence interval [CI], .59–.85) and 0.58 (95% CI, .46–.73), respectively; pooled estimates for all-cause hospitalization and laboratory-confirmed influenza were not statistically significant. The cohort and case-control studies indicated significant protective associations for influenza-like illness and laboratory-confirmed influenza. No studies reported harms to patients. Using GRADE, the quality of the evidence for the effect of HCP vaccination on mortality and influenza cases in patients was *moderate* and *low*, respectively. The evidence quality for the effect of HCP vaccination on patient hospitalization was *low*. The overall evidence quality was *moderate*.

Conclusions. The quality of evidence is higher for mortality than for other outcomes. HCP influenza vaccination can enhance patient safety.

Keywords. decision making; evidence-based medicine; health personnel; influenza vaccines; quality of healthcare.

Influenza vaccination of healthcare personnel (HCP) is recommended in the United States and in >40 other countries [1, 2]. Infected HCP may transmit influenza to patients, many of whom have serious underlying conditions that increase the risk of complications [3]. There is, however, controversy surrounding the evidence that HCP influenza vaccination reduces morbidity and mortality among patients [4–6]. Of 2 recent systematic reviews, 1 concluded that there is likely a protective effect for patients in long-term care settings [6], and the other concluded that there is a lack of evidence [5]. The main controversies centered on the appropriateness of nonspecific patient outcomes and the quality of the overall body of evidence.

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Our objectives were to conduct a systematic review and to grade the quality of evidence to ascertain the effect of influenza vaccination of HCP on morbidity and mortality in patients of healthcare facilities.

METHODS

Search Strategy

We conducted electronic searches of Medline, Embase, CINAHL, Web of Science, and the Cochrane Library for studies published from 1948 through June 2012. Search terms are provided in Supplementary Table 1. We searched for additional studies by scanning references of included studies as well as relevant reviews.

Study Selection and Data Extraction

We included randomized controlled trials, cohort studies, and case-control studies published in any language that reported the association between vaccination of HCP with inactivated influenza vaccine or live attenuated influenza vaccine (LAIV) and morbidity/mortality in patients of healthcare facilities. Two reviewers (M.C.L. and N.A.) selected studies in 2 stages: review of titles and abstracts, then review of full-text articles. Discrepancies or disagreements were resolved through discussion between the 2 reviewers or with a third reviewer (F.A.). Three reviewers (M.C.L., N.A., F.A.) independently extracted data from eligible full-text articles using standardized forms and graded the quality of evidence; any disagreements were resolved by discussion. We did not contact study authors for additional information.

Grading Quality of Evidence

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology for grading the quality of evidence [7]. GRADE is used by >60 organizations worldwide, including the US Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices, the National Institute of Health and Clinical Excellence (United Kingdom), the Norwegian Directorate of Health, the Robert Koch Institute (Germany), and the World Health Organization [8].

Grading quality of evidence begins with the study design. The initial evidence grade is classified as *high* for randomized controlled trials (RCTs) and *low* for observational studies. There are 5 GRADE criteria for downgrading the evidence grade: risk of bias, inconsistency, indirectness, imprecision, and publication bias. There are 3 GRADE criteria for upgrading the evidence grade: large magnitude of effect, dose-response, and opposing residual confounding or bias. These criteria determine the final classification into 4 evidence grades (*high*, *moderate*, *low*, or *very low*) [9]. The evidence grades reflect confidence in effect estimates.

For assessing risk of bias for cluster randomized trials, we used a tool developed by the Cochrane Collaboration that includes consideration of the following biases: recruitment bias, baseline imbalance, loss of clusters (including missing outcomes for individuals within clusters), and failure to account for clustering in analysis [10]. For assessing risk of bias for cohort and case-control studies, we used the Newcastle-Ottawa Scale [11].

We selected and ranked patient outcomes in terms of their importance for making a recommendation [9]. Using a modified Delphi process, we (F.A., N.A., M.C.L., C.M.W.) ranked outcomes into 3 categories prior to extracting data and grading the evidence: critical to decision making—mortality, hospitalization, cases of influenza; important but not critical to decision making—length of hospital stay, adverse events related to possible transmission of live attenuated influenza virus to immunocompromised patients by HCP vaccinated with LAIV; and low importance—number of days of influenza illness. We present the quality of evidence for outcomes that were considered to be critical to decision making.

Statistical Analysis

For the cluster randomized trials, we performed meta-analysis using Review Manager software [12]. Because of differences across trials in patient characteristics and HCP influenza vaccination rates, as well as varying outcome definitions and follow-up periods, we used the random effects model (inverse variance method). We computed pooled risk ratios and assessed statistical heterogeneity using the χ^2 and I^2 statistic. Pooled risk difference estimates may not be meaningful because risk difference is very sensitive to the control group risk, and control group risk may differ substantially between studies [13]. Therefore, we computed risk difference using GRADEPro software for a range of control group risks [8]. Risk difference was calculated by subtracting the assumed control group risk from the corresponding intervention group risk. The corresponding intervention group risk (and its 95% confidence interval [CI]) was derived by multiplying the assumed control group risk by the pooled risk ratio (and its 95% CI). For calculating relative risk reduction, we used the following formula: relative risk reduction = $(1 - \text{pooled risk ratio}) \times 100$ [14]. We conducted subgroup analysis, which was not prespecified in our study protocol, to assess the effect of potential residual confounding. Our analyses took into account clustering associated with randomization at the facility level: We recalculated the standard error of the effect estimate at the study level ignoring clustering and then multiplied by the square root of the design effect [10]. We used design effects that were cited in a previous systematic review [5]. We did not perform meta-analysis of the cohort and case-control studies because of differing analysis methods and units.

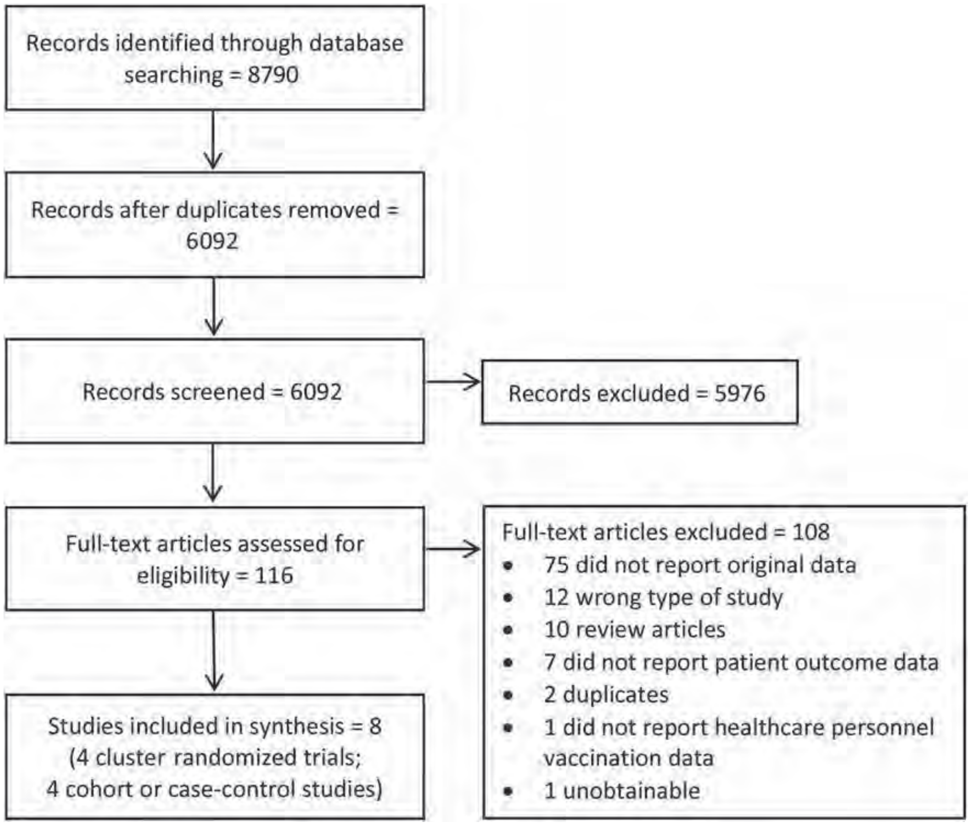

Figure 1. Study selection for review of evidence on effect of influenza vaccination of healthcare personnel.

RESULTS

Study Selection

Our literature search identified 8790 articles. After removing duplicates, we screened 6092 articles (Figure 1). Four cluster randomized trials [15–18] and 4 observational studies (2 cohort and 2 case-control studies) [19–22] met the inclusion criteria.

The 4 trials presented data on 116 long-term care facilities that were randomized to HCP influenza vaccination and control arms (Supplementary Table 2). The mean age of patients ranged from 77 to 86 years. Reported HCP vaccination rates ranged from 48% to 70% in the intervention arms and 5% to 32% in the control arms. The follow-up period was the entire influenza season for 2 trials [15, 18], and was confined to the period of influenza activity for the remaining 2 trials [16, 17]. Among the 4 observational studies, 3 were conducted in long-term care settings (total of 234 facilities); 1 study was done in a hospital setting.

Effect Estimate

The pooled risk ratio across the cluster randomized trials for all-cause mortality was 0.71 (95% CI, .59–.85), indicating a 29% (95% CI, 15%–41%) reduction in deaths (Figure 2). For influenza-like illness, the pooled risk ratio and relative risk reduction were 0.58 (95% CI, .46–.73) and 42% (95% CI, 27%–54%), respectively. The pooled risk ratios for all-cause hospitalization and laboratory-confirmed influenza were not statistically significant. There was low statistical heterogeneity for all outcomes.

The risk difference (ie, absolute risk reduction) for each outcome associated with the mean control group risk, as well as assumed low and high values of control group risk, is shown in Table 1 and Supplementary Table 3. For example, the risk difference for all-cause mortality was 44 fewer deaths per 1000 patients when the control group risk was 151 deaths per 1000 patients (Table 1); the risk difference was 17 fewer deaths per 1000 when the assumed control group risk was 60 per 1000 (Supplementary Table 3).

The results of observational studies showed that HCP influenza vaccination was associated with a lower risk of influenza-like illness (Table 2). Significant protective associations were also reported for laboratory-confirmed influenza.

Subgroup Analysis

Because of concern that residual confounding from other pathogens (eg, respiratory syncytial virus, parainfluenza viruses) could have resulted in overestimation of the effect on reducing patient mortality [5], we conducted subgroup analysis based on the period of follow-up. For the subgroup with follow-up periods comprising the entire influenza season, the pooled risk

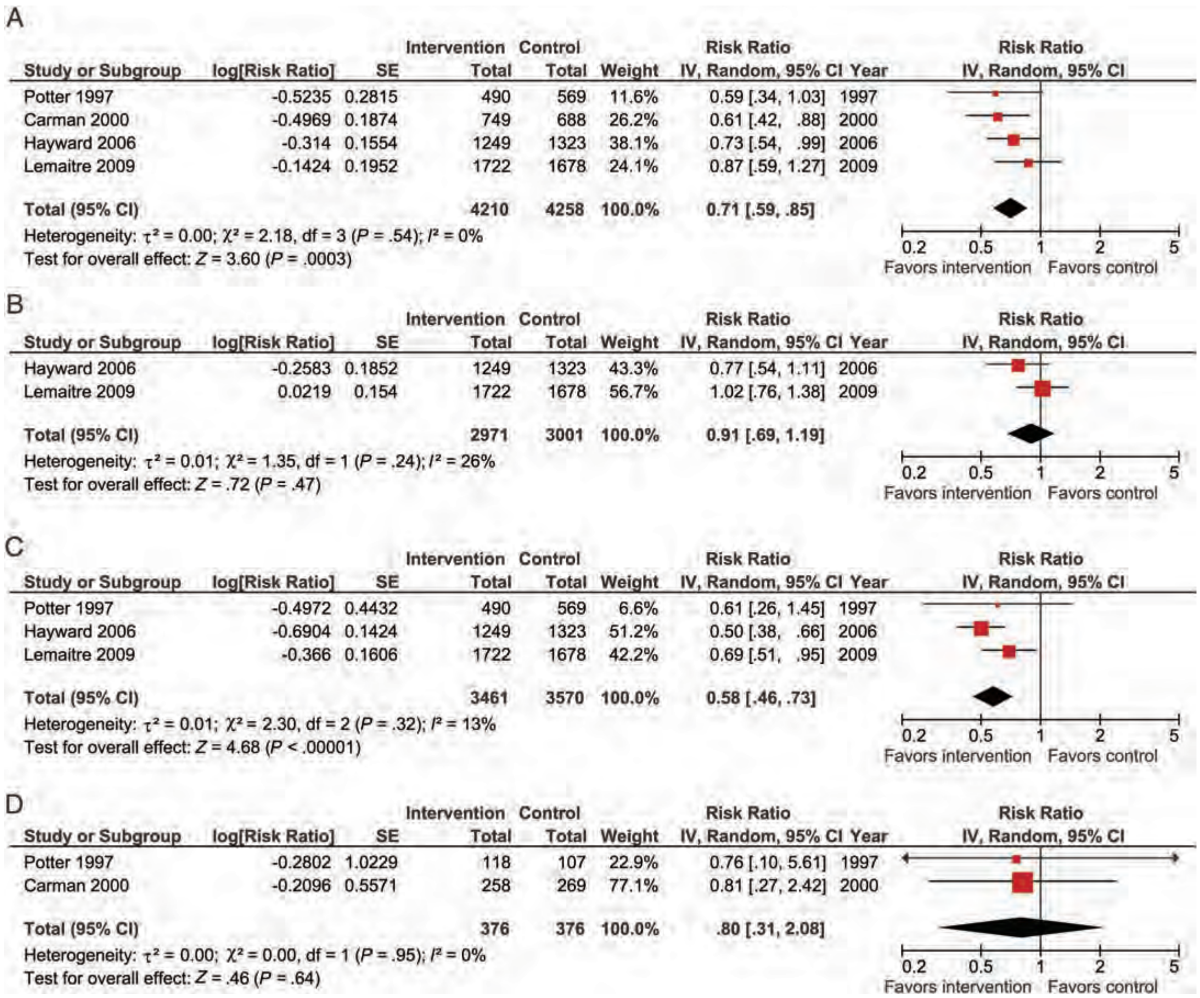

Figure 2. Effect of influenza vaccination of healthcare personnel on patient outcomes: forest plots of cluster randomized trials. *A*, All-cause mortality. *B*, All-cause hospitalization. *C*, Influenza-like illness. *D*, Laboratory-confirmed influenza A or B. Study-level and pooled risk ratios are adjusted for clustering. Abbreviations: CI, confidence interval; IV, inverse variance; SE, standard error.

Table 1. Effect of Influenza Vaccination of Healthcare Personnel: Findings of Cluster Randomized Trials[a]

Outcome Among Patients	No. of Patients (Studies)	Assumed Risk in Control Group per 1000[b]	Corresponding Risk in Intervention Group per 1000 (95% CI)	Pooled Risk Ratio (95% CI)[c]	Risk Difference per 1000 (95% CI)
All-cause mortality	8468 (4 studies)	151	107 (89–128)	0.71 (.59–.85)	−44 (−23 to −62)
All-cause hospitalization	5972 (2 studies)	95	86 (66–113)	0.91 (.69–1.19)	−9 (−29 to 18)
Influenza-like illness	7031 (3 studies)	162	94 (75–118)	0.58 (.46–.73)	−68 (−44 to −87)
Laboratory-confirmed influenza[d]	752 (2 studies)	64	51 (20–133)	0.80 (.31–2.08)	−13 (−44 to 69)

Abbreviation: CI, confidence interval.

[a] Adjusted for clustering.

[b] Weighted mean control group risk across studies (using weights from meta-analyses).

[c] From meta-analyses (see Figure 2).

[d] Determined using rise in serum antibody titer to influenza A or B among unvaccinated patients [18], or testing of combined nasal and throat swabs by polymerase chain reaction for influenza A and B viruses [15].

Table 2. Effect of Influenza Vaccination of Healthcare Personnel: Description and Findings of Observational Studies

Study	Setting	Analysis	Effect Estimate (95% CI)
Oshitani et al [21]	149 LTCFs, Japan	ILI outbreak (ILIs per week exceeded >10% of patients) in facilities with ≥10 vs <10 vaccinated HCP during December 1998 to March 1999	Crude OR = 0.30 (.09–.69)
Enserink et al [20]	18 LTCFs, Netherlands	ILI incidence among patients in facilities with HCP vaccination rates of ≥15% vs <15% during December 2008 to April 2009	Adjusted rate ratio = 0.3 (.1–1.2)
Wendelboe et al [22]	67 LTCFs, United States	HCP vaccination percentage in facilities with ILI outbreaks (≥1 cases of ILI or laboratory-confirmed influenza[a] in patients) vs no outbreaks during 2006–2007 and 2007–2008 influenza seasons (November–April)	Adjusted OR = 0.82 (.68–.99) for 10 percentage point increase in HCP vaccination
		HCP vaccination percentage in facilities with influenza outbreaks (≥1 cases of laboratory-confirmed influenza[a] in patients) vs no outbreaks	Adjusted OR = 0.76 (.62–.93) for 10 percentage point increase in HCP vaccination
Benet et al [19]	1 hospital (36 units), France	HCP vaccination percentage in unit for cases (ILI patients with laboratory-confirmed influenza[b]) vs controls (ILI patients with negative influenza results) during 2004–2005, 2005–2006, and 2006–2007 influenza seasons (October–April)	Adjusted OR = 0.07 (.005–.98) for ≥35% vs <35% vaccinated HCP in unit

Abbreviations: CI, confidence interval; HCP, healthcare personnel; ILI, influenza-like illness; LTCF, long-term care facility; OR, odds ratio.

[a] Determined using viral culture and rapid influenza antigen detection test.

[b] Nasal swabs tested for influenza virus by immunocapture enzyme-linked immunosorbent assay, immunostaining, tissue cell culture, and polymerase chain reaction.

ratio and the relative risk reduction were 0.60 (95% CI, .44–.82) and 40% (95% CI, 18%–56%), respectively. For the subgroup with follow-up periods confined to the period of influenza activity, the pooled risk ratio was 0.78 (95% CI, .62–.99) and the relative risk reduction was 22% (95% CI, 1%–38%).

Quality of Evidence

The quality of evidence from randomized trials for the effect of HCP vaccination on mortality among patients was *moderate* (Table 3, Supplementary Table 4). The quality of evidence was downgraded because of indirectness, as all-cause mortality is a surrogate for influenza-specific mortality. The quality of evidence for the effect on hospitalization was downgraded by 2 levels to *low* because of indirectness and imprecision.

For the effect on influenza cases, evidence was graded for both the surrogate outcome of influenza-like illness and the specific outcome of laboratory-confirmed influenza. For influenza-like illness, the quality of evidence from randomized trials was *low* and that from observational studies was *very low* (downgraded because of risk of bias and indirectness). For laboratory-confirmed influenza, the evidence quality from randomized trials was *very low* (risk of bias and imprecision) and that from observational studies was *low* (none of the criteria for upgrading the initial evidence quality of *low* for observational studies were determined to be applicable).

Overall Quality of Evidence

Because the body of evidence for the outcomes of influenza-like illness and laboratory-confirmed influenza comprised both randomized trials and observational studies, the study design that provided higher quality of evidence was selected (Table 4). Therefore, the quality of evidence was *low* for influenza-like illness and *low* for laboratory-confirmed influenza. The quality of evidence for the effect on influenza cases was *low*, regardless of whether influenza-like illness or laboratory-confirmed influenza was used as the basis for grading. The quality of evidence for the effect on hospitalization was *low*, and that for mortality was *moderate*. The overall quality of evidence is determined by the quality of evidence for mortality if reduction in mortality alone is sufficient to support HCP influenza vaccination. Therefore, the overall quality of evidence across outcomes was *moderate* (Table 4), as mortality was considered a critical outcome for decision making.

DISCUSSION

Our results indicate that the quality of evidence that HCP influenza vaccination reduces mortality and influenza cases in patients of healthcare facilities is *moderate* and *low*, respectively. The quality of evidence for the finding that there is no effect of HCP vaccination on hospitalization is *low*. The overall quality of evidence is *moderate*.

Our study has potential limitations. First, our ranking of outcomes may not represent the views of guideline panels that make vaccination recommendations. However, none of the studies reported data on outcomes we classified as noncritical. We did not consider the outcomes length of hospital stay and

Table 3. Effect of Influenza Vaccination of Healthcare Personnel: Quality of Evidence

Outcome Among Patients	Design (No. of Studies)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations[a]	Quality of Evidence (GRADE)
Mortality	RCT (4)	Not serious	No serious	Serious[b]	No serious	None	Moderate
Hospitalization	RCT (2)	Not serious	No serious	Serious[b]	Serious[c]	None	Low
Influenza-like illness	RCT (3)	Serious[d]	No serious	Serious[b]	No serious	None	Low
Influenza-like illness	OBS (3)	Serious[e]	No serious	Serious[b]	No serious	None	Very low
Laboratory-confirmed influenza	RCT (2)	Very serious[f]	No serious	No serious	Serious[g]	None	Very low
Laboratory-confirmed influenza	OBS (2)	No serious	No serious	No serious	No serious	None	Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; OBS, observational study; RCT, randomized controlled trial.

[a] Strength of association, dose response, opposing plausible residual confounding or bias, publication bias.

[b] The study outcomes all-cause mortality, all-cause hospitalization, and influenza-like illness are surrogates for influenza-specific mortality, influenza-specific hospitalization, and influenza cases, respectively.

[c] The 95% confidence interval of the pooled risk ratio includes both no effect and appreciable benefit.

[d] Completeness of assessing influenza-like illness in intervention and control groups was unclear.

[e] Completeness of assessing influenza-like illness and healthcare personnel vaccination was unclear.

[f] Completeness of obtaining patients' samples for laboratory confirmation of influenza was low or differed between intervention and control groups. Intervention and control groups were not well matched for patients' Barthel disability scores in 1 of the 2 studies.

[g] Sample size was small (effective sample size was less than study sample size because of clustering).

number of days of influenza illness to be critical because these are similar in concept to the outcomes hospitalization and cases of influenza, respectively. We are not aware of any studies

Table 4. Effect of Influenza Vaccination of Healthcare Personnel: Overall Quality of Evidence

Outcome Among Patients	Study Design (No. of Studies)	Finding	Quality of Evidence (GRADE)	Overall Quality of Evidence[a] (GRADE)
Mortality	RCT (4)	Reduces mortality	Moderate	Moderate
Hospitalization	RCT (2)	No effect on hospitalization	Low	
Influenza[b]				
Influenza-like illness	RCT (3)[c]	Reduces influenza-like illness	Low	
Laboratory-confirmed influenza	OBS (2)[c]	Reduces laboratory-confirmed influenza	Low	

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; OBS, observational study; RCT, randomized controlled trial.

[a] If reduction in mortality alone among patients is sufficient to support influenza vaccination of healthcare professionals, the overall quality of evidence is determined to be moderate.

[b] Quality of evidence for the effect on influenza cases is low, regardless of whether influenza-like illness or laboratory-confirmed influenza is used as the basis for grading.

[c] Body of evidence for outcome includes both RCTs and observational studies; the study design that provides higher quality of evidence was selected.

that reported transmission of vaccine virus from LAIV recipients in healthcare settings. We considered the theoretical harm of transmission to be important but not critical for decision making. Second, pooled risk ratio estimates from the trials indicated a 29% reduction in all-cause mortality among long-term care patients. This finding may be questioned because influenza has been estimated to contribute to <10% of all winter deaths among persons aged 65 years and older [5, 23]. However, no estimates are available on the proportion of winter deaths attributable to influenza among frail elderly patients residing in long-term care settings. Although the facilities were randomized, we cannot rule out the possibility of residual confounding due to different patterns of circulation of pathogens within intervention and control facilities [17]. Our subgroup analysis limited to the period of influenza activity, when the potential for residual confounding due to other pathogens would likely be lower [24–26], showed a 22% reduction in all-cause mortality with very wide confidence intervals. Finally, influenza-specific outcomes provide the most relevant evidence [27, 28]. Use of nonspecific outcomes, assuming adequate control of confounding factors, leads to underestimation of true vaccine effectiveness [28]. The study outcomes of all-cause mortality and all-cause-hospitalization were downgraded for indirectness because these outcomes are surrogates for influenza-specific mortality and influenza-specific hospitalization, respectively. It would have been preferable to have data on influenza-specific mortality and hospitalization, but direct ascertainment of these specific outcomes is problematic because of the difficulty of distinguishing whether hospitalizations

and deaths due to exacerbation of chronic illnesses and other conditions are attributable to the complications of influenza or to other reasons; estimates of influenza-associated mortality and hospitalization are usually computed at the population level using statistical modeling techniques [29, 30]. For influenza cases, study data were available for the surrogate outcome of influenza-like illness and the specific outcome of laboratory-confirmed influenza. However, the quality of evidence was *low* regardless of outcome.

Two cluster randomized trials reported data on laboratory-confirmed influenza, but the quality of the evidence was determined to be *very low*. The real-life challenges and resource intensiveness of obtaining samples, as well as the limitations of laboratory methods, contributed to this determination. The sample size in 1 study was reduced because of the need to exclude vaccinated patients from the analysis (a rise in antibody titer to influenza can be due to either vaccination or infection); furthermore, only 43% of the eligible unvaccinated patients provided paired blood samples [18]. The other study selected a random sample of 50% of patients for conducting nasal and throat swabs taken at 2-week intervals during the peak influenza period; swabs were obtained from 69% of the intervention group and 78% of the control group [15].

Our study differs from previous systematic reviews of the effect of HCP influenza vaccination on protection of patients in 3 main ways: (1) Our assessment of the quality of evidence was based on the GRADE method used by numerous organizations for developing evidence-based recommendations; (2) we present the quality of evidence for each individual outcome; and (3) we used a tool that has been specifically designed by the Cochrane Collaboration to assess risk of bias in cluster randomized studies. The 2 recent systematic reviews included the same 4 cluster randomized trials that we reviewed, but assessed risk of bias using a Cochrane Collaboration tool that was primarily designed to assess risk of bias in trials where individuals rather than facilities are randomized [5, 6]. There were differences in the types and numbers of observational studies reviewed. One review also included cross-sectional and ecologic studies [6], but we decided a priori to exclude such study designs due to their inherent weaknesses. The other review had inclusion criteria similar to ours, but only 1 cohort study was available at the time of their review [5].

Several facts support the biological plausibility of HCP vaccination to reduce influenza among patients: A substantial proportion of HCP become infected with influenza virus during influenza seasons [31–33]; infected persons can shed virus before the onset of symptoms and during subclinical or clinical illness [34]; many HCP with influenza illness continue to work [31, 32, 35]; and influenza vaccination reduces laboratory-confirmed influenza among healthy adults (which includes most HCP) [36]. However, the role of competing sources of transmission, such as visitors and new patients, needs to be considered. Modeling studies indicate that the relative effect of HCP vaccination on influenza infection among patients is lower in the hospital than in long-term care settings, which may be attributed in part to the relatively greater role of competing sources of transmission in hospitals [37, 38]. Nonetheless, because of higher expected attack rates in hospital patients compared to long-term care patients, the absolute risk reduction in hospital patients may be higher [38]. Such modeling studies are useful when there is a paucity of direct evidence for all parameters of interest. We were not able to assess the effect of HCP vaccination in ambulatory settings as no published studies in these settings met our inclusion criteria.

For any clinical question, the quality of evidence will vary based on the question and the context, and the best available evidence should be used for developing recommendations. An evidence-based approach for developing recommendations requires transparency concerning the evidence and transparency in how judgments regarding the quality of evidence were made. Key factors for developing recommendations include the quality of evidence, balance of benefits and harms, values and preferences, and health economic analyses [7, 39]. The benefits of HCP influenza vaccination, which include likely reduction in morbidity and mortality among patients and reduction in illness among HCP themselves, outweigh possible harms. HCP influenza vaccination can enhance patient safety.

Postscript: A cluster randomized trial published in June 2013 reported that HCP influenza vaccination was associated with decreased influenza and/or pneumonia in hospital patients [40]. However, this study does not change our assessment of the quality of the body of evidence, as its quality is similar to studies on influenza outcomes included in our review.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Effect of Influenza Vaccination of Nursing Home Staff on Mortality of Residents: A Cluster-Randomized Trial

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OBJECTIVES: To evaluate the effect of staff influenza vaccination on all-cause mortality in nursing home residents.

DESIGN: Pair-matched cluster-randomized trial.

SETTING: Forty nursing homes matched for size, staff vaccination coverage during the previous season, and resident disability index.

PARTICIPANTS: All persons aged 60 and older residing in the nursing homes.

INTERVENTION: Influenza vaccine was administered to volunteer staff after a face-to-face interview. No intervention took place in control nursing homes.

MEASUREMENTS: The primary endpoint was total mortality rate in residents from 2 weeks before to 2 weeks after the influenza epidemic in the community. Secondary endpoints were rates of hospitalization and influenza-like illness (ILI) in residents and sick leave from work in staff.

RESULTS: Staff influenza vaccination rates were 69.9% in the vaccination arm versus 31.8% in the control arm. Primary unadjusted analysis did not show significantly lower mortality in residents in the vaccination arm (odds ratio = 0.86, $P = .08$), although multivariate-adjusted analysis showed 20% lower mortality ($P = .02$), and a strong correlation was observed between staff vaccination coverage and all-cause mortality in residents (correlation coefficient = -0.42, $P = .007$). In the vaccination arm, significantly lower resident hospitalization rates were not observed, but ILI in residents was 31% lower ($P = .007$), and sick leave from work in staff was 42% lower ($P = .03$).

CONCLUSION: These results support influenza vaccination of staff caring for institutionalized elderly people. **J Am Geriatr Soc 57:1580–1586, 2009.**

Key words: elderly; nursing homes; residents; staff influenza vaccination

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Influenza is a leading cause of death in older adults.[1] In developed temperate countries, influenza accounts for an average excess all-cause mortality of approximately 5% during winter in the elderly population.[2] Influenza vaccination is an effective means of preventing cases of influenza in children aged 2 and older and healthy adults,[3–5] but in elderly people, influenza vaccination is less effective against influenza or influenza-like illness (ILI), although well-matched vaccines still prevent serious events from pneumonia and influenza and reduce all-cause mortality by 40% to 60%.[6] However, despite high levels of immunization, there have been reports of influenza outbreaks in homes for elderly individuals.[7–11] Vaccination of persons caring for elderly people has therefore been recommended to limit transmission, yet nearly 50% of French nursing homes have a staff influenza vaccine coverage rate less than 40%.[12]

Two randomized controlled trials have suggested that staff influenza vaccination can reduce mortality in elderly residents of long-term care facilities.[13,14] These findings must be interpreted with caution given the presence of selection and performance bias.[15] More recently, a group-randomization trial conducted in nursing homes showed 27% lower all-cause mortality and 50% lower ILI rates in

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the vaccination arm than the control arm during the first year of the study but no benefit the following year.[16]

The current study examined the effect of staff influenza vaccination on all-cause mortality in institutionalized elderly people and on morbidity in residents and staff.

MATERIAL AND METHODS

Study Design

A cluster-randomized controlled trial was conducted in which 40 nursing homes matched in pairs were randomly allocated to a vaccination (intervention) arm or a no-intervention control arm. The Saint-Germain-en-Laye hospital ethics committee (June 16, 2006; 06046) and the French Data Protection Authority (907162) approved the study.

This study focused on nursing homes housing between 50 and 200 seniors, corresponding to 376 of the 1,105 nursing homes listed in the Paris area at the time of the study. Each of these 376 nursing homes was sent a written invitation to participate, and 88 responded positively. Of these, 40 nursing homes in which the staff influenza vaccination coverage rate was less than 40% during the 2005/06 winter season were selected. Each institution was then pair-matched for the following characteristics: size, staff vaccination coverage rate in 2005/06 (0–20% or 20–40%), and Group Iso Resources (GIR) weighted-average score. The GIR score is used in France as a disability index for institutionalized elderly people and takes into account degrees of physical and mental autonomy. The score is based on the Table of Geriatric Autonomy GIR and is measured in all institutionalized elderly people twice a year.[17] The scores range from 1 (severe disability) to 6 (total autonomy). Only residents aged 60 and older who were in the nursing home at the beginning of the study or who were admitted during the overall study period were included. The study started on December 4, 2006, and ended on April 1, 2007.

Methods

Randomization was centralized and based on a simple computerized random number generator. In the intervention arm, a promotional campaign based on posters, leaflets, and an information meeting with the study team between September 15 and October 31, 2006, first sensitized staff to the benefits of influenza vaccination. The campaign described the potential benefits of influenza vaccination for one's own protection and that of the residents. Influenza vaccination was further recommended during face-to-face interviews with each member of staff present in the nursing homes between November 6 and December 15, 2006. The study team individually met all administrative staff, technicians, and caregivers to invite them to participate, and volunteers were vaccinated at the end of the interview. During the interview, prior vaccination status and, if appropriate, the reason for nonvaccination were also collected. The vaccine was an inactivated preparation (Influvac, Solvay Pharma Laboratory, Suresnes, France) containing 15 μg each of strains A/Wisconsin/67/2005-like (H3N2), A/New Caledonia/20/99 (H1N1), and B/Malaysia/2506/2004.

In the control arm, only routine information on influenza vaccination was provided. No particular instruction was given regarding hygiene and infection control practices (e.g., use of masks, handwashing, isolation, or use of antivirals for treatment or prophylaxis) in either arm. The numbers of residents leaving the nursing homes permanently or temporarily were recorded. Investigating physicians entered data online using an electronic form designed specifically for the study.

The extent of vaccination coverage in the control arm and information regarding sick leave for staff in both arms were determined with a questionnaire sent to all staff at the end of the study.

Rapid diagnostic tests (Quick View Influenza Test; Quidel Corp., San Diego, CA) were distributed to each nursing home for use when clusters of ILI occurred in residents. When suspected clusters occurred, a team of monitors was sent to the nursing home to document signs and symptoms in all residents and staff and to record the results of the rapid diagnostic tests and neuraminidase inhibitor prescriptions given to residents.

Analysis

The influenza epidemic period was defined as a weekly ILI incidence of more than 127 cases per 100,000 inhabitants, as reported by the Sentinelles General Practitioners Network.[18] A moderate influenza epidemic was reported in the general French community between January 15, 2007, and March 4, 2007, predominantly due to A/Wisconsin/67/2005-like (H3N2) strains.[19] For the purposes of this study, the primary study period was defined as the period starting 2 weeks before and ending 2 weeks after the observed epidemic (January 1, 2007 to March 18, 2007). The primary endpoint was total mortality rate during the primary study period.

Secondary endpoints were the incidence rates of hospitalization and ILI in residents during the primary study period. ILI was defined as a fever of 37.8°C or more and onset of respiratory symptoms or worsening of chronic respiratory conditions. Another secondary endpoint was the proportion of staff who reported at least 1 day of sick leave.

Sample Size

An influenza epidemic period lasting 2 months, an expected mortality rate of 8% in the control arm,[20] a 40% reduction in all-cause mortality rate in residents after staff vaccination (expected mortality rate in the intervention arm of 4.8%), and two-sided hypothesis testing were assumed.[15] The intrapair coefficient of variation of all-cause mortality was set at 0.3,[21] and the median size of the nursing homes was set at 100 residents (range 50–200). Twenty pairs of nursing homes were necessary to obtain a power of 80% with 2,000 residents in each group. The effect size of this design was 1.9.

Statistical Methods

The analyses included all residents who were present on at least 1 day in a participating nursing home between the beginning and end of the primary study period. All analyses were done on an intention-to-treat basis. To compare study outcomes between arms, a cluster-specific method was used, because nursing homes rather than residents were randomized. The analysis was performed considering that

outcomes were measured at the individual resident level. Odds ratios were calculated using alternating logistic regression, with one-nested log odds ratios to model the association between responses of the same pair and the same nursing home within the pair.[22,23] The primary analysis, as specified in the protocol, was a univariate estimate of the effectiveness of the intervention on mortality. In secondary analyses, multivariate estimates were adjusted for the residents' age, vaccination status, GIR disability score, and Charlson comorbidity index. The GIR disability score was used instead of the Barthel disability score, because French physicians had greater experience with it, the Barthel score was missing for all residents in one nursing home, and introducing the Barthel score in the multivariate analysis did not change the results (not shown). Missing vaccination status and Charlson comorbidity index values were imputed using a Bayesian multiple imputation procedure with 10 replicates. Correlation between staff vaccination coverage and all-cause mortality was tested using the Spearman correlation coefficient. Statistical tests were two tailed, with a type I one error of 5%. Statistical analyses were performed with SAS software version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

The total number of residents present in the participating nursing homes during the overall study was 3,483: 1,751 in the vaccination arm and 1,732 in the control arm. There were 3,400 residents during the primary study period: 1,722 in the vaccination arm and 1,678 in the control arm (Figure 1). The average staff influenza vaccination rate was 69.9% in the vaccination arm (range 48.4–89.5%). Five hundred sixty-six (55.8%) vaccination questionnaires were collected in the control arm and 448 (45.3%) in the vaccination arm. The average staff influenza vaccination rate was 31.8% in the control arm (range 0–69.0%). No serious adverse events were attributed to vaccination. Stated reasons for not being vaccinated were distributed similarly in the two arms, as follows: fear of vaccine adverse effects (53.4%), belief that vaccination is not effective (31.3%), preference for other modes of influenza prevention (12.3%), and contraindications (3.0%).

The characteristics of the residents in the two arms were similar, with a mean age of 86, a majority of women (77.4%), an average GIR disability score of 2.92, an average Barthel disability score[24] of 43.4, an average Charlson comorbidity index[25] of 2.34, and a vaccination coverage rate of 91.8% for the 2006/07 winter season in residents whose vaccination status was known (Table 1). The only significant difference was a higher proportion of residents vaccinated against pneumococci during winter 2005/06 in the control arm owing to 100% vaccine coverage in two control nursing homes. After removing the two pairs including these homes, the difference was no longer significant.

The primary analysis—an unadjusted analysis restricted to the primary study period—showed no significant difference in mortality in the vaccination arm than in the control arm (Table 2, odds ratio (OR) = 0.86, 95% confidence interval (CI) = 0.72–1.02). Likewise, there was no difference in mortality from respiratory causes, although mortality from cardiovascular causes was lower in the vaccination arm. The incidence of hospital admissions did not differ between the arms. In contrast, the incidence of ILI was significantly lower in the vaccination arm.

In the vaccination arm, 8.7% of staff reported at least 1 day of sick leave during the primary study period, versus

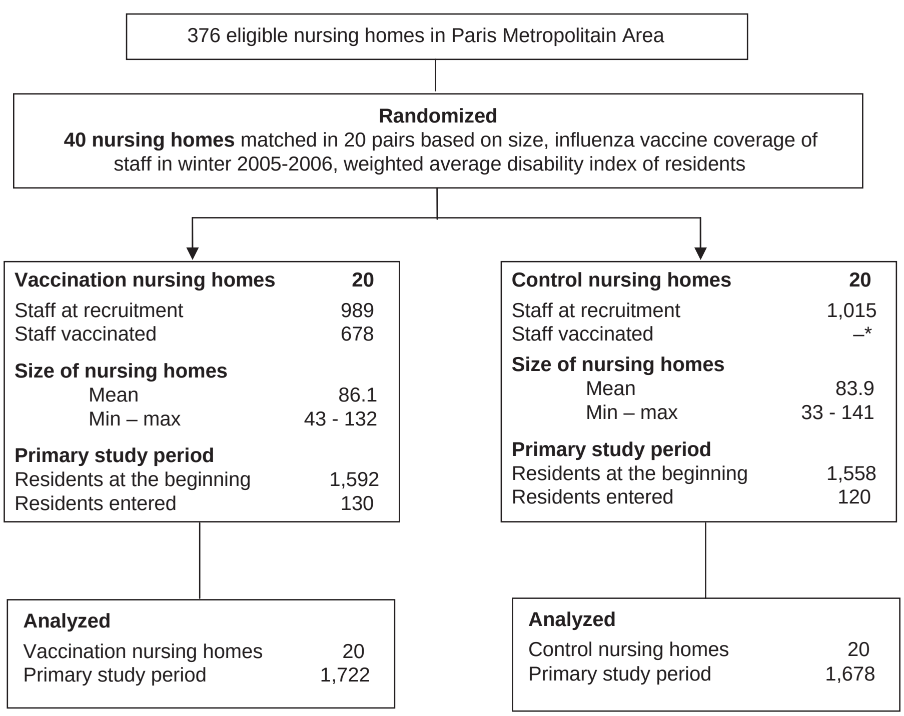

Figure 1. Flow chart.
*Immunization coverage was estimated at the end of the overall study period.

Table 1. Characteristics of the Nursing Home Residents

Characteristic	Vaccination Arm (n = 1,722)	Control Arm (n = 1,678)
Age, mean ± SD	86.1 ± 8.4	86.0 ± 8.7
Female, n (%)	1,334 (77.5)	1,282 (76.4)
Group Iso Resources disability score, mean ± SD	2.95 ± 1.44	2.90 ± 1.45
Barthel disability score, mean ± SD*	42.8 ± 34.8	44.6 ± 34.6
Charlson Comorbidity Index, mean ± SD†	2.35 ± 1.95	2.33 ± 1.75
Influenza vaccination, winter 2006/07, n (%)		
Yes	1,452 (84.3)	1,385 (82.5)
No	150 (8.7)	103 (6.1)
Unknown‡	120 (7.0)	190 (11.3)
Influenza vaccination, winter 2005/06, n (%)		
Yes	961 (57.3)	985 (57.2)
No	96 (5.7)	143. (8.3)
Unknown‡	621 (37.0)	594 (34.5)
Documented pneumococcal vaccination, 2005, n (%)	59 (3.4)	222 (13.2)§

* Pair 19 not considered, data not available.
† Pairs 19, 12, and 14 not considered, data not available in three nursing homes.
‡ No written information on vaccination status in the medical files.
§ Two nursing homes with 100% vaccination in the control arm.
SD = standard deviation.

13.3% in the control arm (OR = 0.58, 95% CI = 0.36–0.96, $P = .03$), although in the control arm, vaccinated staff were more likely than unvaccinated staff to take sick leave (36/175 (20.6%) vs 39/388 (10.0%), $P < .001$).

Multivariate-adjusted analysis identified a significant difference in all-cause mortality between the arms during the primary study period (Table 3, OR = 0.80, 95% CI = 0.66–0.96). Other predictors of mortality were sex, age, Charlson Comorbidity Index, and GIR disability score. Influenza vaccination of residents did not appear to prevent death ($P = .40$). A correlation was observed between staff vaccination coverage and all-cause mortality in residents during the primary study period (Figure 2).

Detailed examination of weekly rates of health outcomes showed that the largest difference in all-cause mortality and ILI between the two arms occurred between December 4, 2006, and January 8, 2007, corresponding to the period from 9 to 4 weeks before the peak of influenza in the community (Supporting Information, Figure S1).

Four ILI clusters were reported in four nursing homes between February 8 and March 13, 2007: three in the control arm and one in the vaccination arm. In two of these outbreaks, the index case was a staff member. The staff vaccination rates in these nursing homes were 7.1%, 33.3%, and 40.9% in the control arm and 55.0% in the vaccination arm. The ILI attack rates in residents were 9.9%, 32.3%, 12.8%, and 12.2%, respectively; 56 residents developed an ILI, of whom 47 had been vaccinated against influenza. Twelve of 25 residents tested for influenza virus were positive. Forty-two residents (75.0%) were treated with oseltamivir, nine were hospitalized (all were treated), and seven died (all were treated).

DISCUSSION

Despite a high staff influenza vaccine coverage rate in the vaccination arm of this study (69.9%), analysis showed no significant effect on all-cause mortality in residents during the primary study period. This may have been due to a lack of power, owing to multiple factors. First, the hypothesis of a 40% lower all-cause mortality may seem "optimistic," compared with the average estimate of 5% of winter deaths that has been found to be attributed to influenza in elderly people.[2] However, this hypothesis was extracted from a recent systematic review on the effectiveness of influenza vaccination for healthcare workers[15] and was consistent with findings of another clustered randomized trial published after the start of the current study.[16] Nevertheless, the 5% all-cause mortality attributable to influenza in a general population aged 65 and older cannot be applied to the institutionalized population of the current study aged 86 years old on average with multiple comorbidities. Conse-

Table 2. Outcomes in the Vaccination and Control Arms During the Primary Study Period (January 1 to March 18, 2007)

Outcome	n (%) Vaccination Arm (n = 1,722)	n (%) Control Arm (n = 1,678)	Odds Ratio* (95% Confidence Interval) Reference = Control	P-Value
Death	89 (5.2)	100 (6.0)	0.86 (0.72–1.02)	.08
Respiratory	19 (1.1)	12 (0.7)	1.55 (0.59–4.10)	.38
Cardiovascular	26 (1.5)	39 (2.3)	0.66 (0.44–0.99)	.045
Other causes	44 (2.6)	49 (3.0)	0.87 (0.84–1.35)	.46
Admission to hospital	150 (8.7)	143 (8.5)	1.03 (0.76–1.40)	.85
Respiratory	29 (1.7)	28 (1.7)	1.01 (0.43–2.34)	.98
Cardiovascular	22 (1.3)	30 (1.8)	0.72 (0.45–1.13)	.15
Other causes	99 (5.7)	85 (5.0)	0.88 (0.78–1.68)	.49
Influenza-like illness	116 (8.7)	163 (11.8)	0.69 (0.52–0.91)	.007

* Alternating logistic regression estimate.
[Correction added after online publication August 4, 2009: the alignment of "Influenza-like illness" has been changed in the Outcome column]

Table 3. Predictors of All-Cause Mortality in Nursing Homes Residents, Winter 2006/07

Variable	Odds Ratio (95% Confidence Interval)	*P*-Value
Sex (male vs female)	1.66 (1.15–2.41)	.008
Arm (vaccination vs control)	0.80 (0.67–0.97)	.02
Age (per 1-year increase)	1.04 (1.02–1.05)	< .001
Charlson Comorbidity Index (per 1-point increment)	1.10 (1.02–1.18)	.01
Group Iso Resources disability score (per 1-point increment)	0.73 (0.64–0.83)	< .001
Influenza vaccination of residents (yes vs no)	0.87 (0.63–1.20)	.40

Alternating logistic regression estimate.

quently, excess optimism did not a priori underpower the initial hypothesis.

However, fewer subjects were included during the primary study period than expected (3,400 vs 4,000), and in the control arm, the mortality rate (6%) was lower than expected (8%), possibly owing to a high vaccine coverage rate in residents (> 80%) or to a high staff vaccine coverage rate in the control arm (31.8% instead of an anticipated value of 10–15%). By comparison with other trials,[13,16] the vaccine coverage rate in the control arm was 6 to 10 times as high in the current study, possibly owing partly to coincidental passage of a bill requiring mandatory influenza vaccination for healthcare workers through the French Senate.[26] Another likely explanation for the lack of power is the moderate nature of the influenza epidemic, and the low accompanying mortality rate, in France and Europe during the 2006/07 winter season.[18,19,27] The French national influenza mortality surveillance system reported only 44 deaths from influenza, of which 16 occurred in nursing homes and seven in long-term care facilities.[28] By comparison, 228 deaths were reported during winter 2004/05.[29] Finally, it has been shown that death attributable to pneumonia and influenza can occur as late as 1 year after the primary episode of pneumonia,[30] and the possibility cannot be excluded that the primary study period was too short to encompass the full mortality burden related to influenza. All these factors may have contributed to undermining the statistical power of the trial.

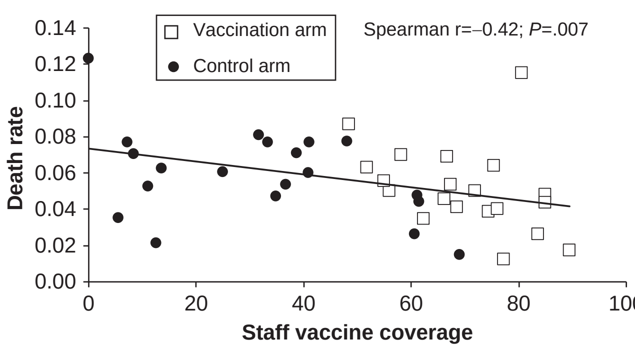

Figure 2. All-cause mortality according to staff vaccine coverage rates during the primary study period (January 1 to March 15, 2007).

In contrast, multivariate analysis showed that belonging to the vaccination arm was a significant independent predictor of mortality in the elderly residents when adjusted for other prognostic factors. Although the intervention and control arms were well balanced with regard to prognostic factors, there were differences in these factors between intervention and control nursing homes belonging to the same pair, possibly accounting for the results of multivariate analysis. Among other potential confounders, the residents' nutritional status—an independent predictor of mortality in elderly people[31]—was not measured in this study. Also, the Charlson Comorbidity Index may not have fully captured the severity of the underlying chronic conditions; other scales (e.g., the Cumulative Illness Rating Scale[32]) might have been more appropriate. It is unclear whether an imbalance between the arms in terms of nutritional status or underlying disease severity would have altered the strength of the observed association between influenza vaccination and mortality in elderly subjects. Nonetheless, this study is the first to show a significant beneficial effect of staff vaccination on mortality in elderly residents of nursing homes after adjustment for other major prognostic factors.

Nevertheless, it was surprising to find that weekly all-cause mortality and ILI incidence rates were clearly lower in the vaccination arm than in the control arm between 9 and 4 weeks before the peak of the influenza epidemic observed in the general community. In the control arm and, to a lesser degree, in the vaccination arm, the total mortality and ILI incidence rates peaked between December 25 and January 7, which coincided closely with the peak circulation of respiratory syncytial virus (RSV) in France. It is therefore likely that some of these deaths and cases of ILI were related to RSV, a virus associated with substantial mortality and morbidity in elderly people,[33,34] although this does not explain why staff influenza vaccination appeared to limit the burden of RSV in nursing homes. In particular, post hoc analyses showed that a few influential pairs of nursing homes did not cause this result (not shown). Among other possibilities, confounding due to lack of blinding may have occurred. The influenza vaccination intervention may have made vaccinated staff more aware of the risks of influenza, leading them to be less exposed to respiratory viruses (including RSV) in the community or to adopt nonspecific preventive measures and thus to be less contagious. Influenza virus may also have circulated in the nursing homes before the national epidemic, but this is unlikely, because the four clusters of cases were all observed during the influenza epidemic period.

Finally, although vaccination of residents did not appear to reduce influenza mortality in this study, the vaccine coverage rate was high, and an imbalance in underlying disease severity might have influenced the results.

This study found that influenza vaccination of staff reduced the incidence of ILI in nursing home residents and sick leave in staff. Multivariate-adjusted analysis identified 20% lower all-cause mortality in the intervention arm, and a significant correlation was observed between staff vaccination coverage and all-cause mortality in residents. The relatively moderate nature of the 2006/07 influenza epidemic and the higher-than-anticipated vaccine coverage rate in the control arm must be taken into account when

interpreting the lack of significantly lower all-cause mortality in residents. Together, these results support influenza vaccination of staff caring for institutionalized elderly people and encourage further evaluation of this practice.

REGISTERING CLINICAL TRIALS

This study was registered with ClinicalTrials.gov, number NCT: 00359554.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Figure S1. Weekly rates of all-cause mortality, hospitalization and influenza-like illness among residents in the two arms. The gray areas indicate the primary study period, which was used for all primary analyses. The black arrows indicate the peaks of respiratory syncytial virus and influenza virus isolation in the community.

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Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant

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ABSTRACT

BACKGROUND

The B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19), has contributed to a surge in cases in India and has now been detected across the globe, including a notable increase in cases in the United Kingdom. The effectiveness of the BNT162b2 and ChAdOx1 nCoV-19 vaccines against this variant has been unclear.

METHODS

We used a test-negative case–control design to estimate the effectiveness of vaccination against symptomatic disease caused by the delta variant or the predominant strain (B.1.1.7, or alpha variant) over the period that the delta variant began circulating. Variants were identified with the use of sequencing and on the basis of the spike (S) gene status. Data on all symptomatic sequenced cases of Covid-19 in England were used to estimate the proportion of cases with either variant according to the patients' vaccination status.

RESULTS

Effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) was notably lower among persons with the delta variant (30.7%; 95% confidence interval [CI], 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7); the results were similar for both vaccines. With the BNT162b2 vaccine, the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant. With the ChAdOx1 nCoV-19 vaccine, the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant.

CONCLUSIONS

Only modest differences in vaccine effectiveness were noted with the delta variant as compared with the alpha variant after the receipt of two vaccine doses. Absolute differences in vaccine effectiveness were more marked after the receipt of the first dose. This finding would support efforts to maximize vaccine uptake with two doses among vulnerable populations. (Funded by Public Health England.)

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India has experienced a surge in cases of coronavirus disease 2019 (Covid-19) since late March 2021, reaching more than 400,000 cases and 4000 deaths reported each day in early May 2021.[1] This increase has resulted in hospital services becoming overwhelmed and in a scarcity of oxygen supplies.[2] Although only a small proportion of samples have been sequenced, B.1.617 lineages of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have dominated. The B.1.617.2 (delta) variant was first detected in India in December 2020 and became the most commonly reported variant in the country starting in mid-April 2021.[1] As of May 19, 2021, the variant had been detected in 43 countries across six continents in GISAID (originally an acronym for global initiative on sharing avian influenza data but more recently a site for compiling sequence data on viruses, particularly influenza and coronaviruses, that threaten to cause a pandemic).[3] In the United Kingdom, a rapid increase in cases with this variant has been seen associated with travel from India and with community transmission.[4]

In the United Kingdom, vaccination was initially prioritized for older adults, caregivers, and health and social care workers, with subsequent rollout to persons in clinical risk groups and younger-age cohorts.[5] At an early stage of the rollout, a policy decision, based on advice from the Joint Committee on Vaccination and Immunisation, was made to use an extended administration interval of up to 12 weeks in order to maximize the number of vulnerable persons receiving the first dose during the second wave of the pandemic in the context of constraints on vaccine supply and delivery.[6]

Vaccines have been found to be highly efficacious at preventing symptomatic disease, as shown by clinical trials[7-9] and real-world evidence.[10-14] The B.1.1.7 (alpha) variant, first identified in the United Kingdom, was the predominant lineage seen between January and May 2021. Levels of protection against the alpha variant that are conferred by vaccination are similar to those observed in clinical trials, with additional protection against severe disease.[10,11,15-17] Laboratory data indicate that the B.1.351 (beta) variant has reduced neutralization, according to analysis of serum samples obtained from vaccinated persons.[18,19] Observational data from Qatar indicated modestly reduced effectiveness against symptomatic disease caused by this variant but high levels of effectiveness against severe, critical, or fatal disease in persons vaccinated with the BNT162b2 vaccine (Pfizer–BioNTech).[17] Furthermore, a trial of the NVX-CoV2373 vaccine (Novavax) showed 51.0% efficacy against the beta variant.[20] Finally, high levels of neutralization have been seen with the P.1 (gamma) variant in serum samples obtained from persons vaccinated with the BNT162b2 vaccine, and one study showed only minimally reduced vaccine effectiveness against test-positive cases with one dose of messenger RNA vaccine.[19,21,22]

The delta variant is characterized by the spike protein mutations T19R, Δ157-158, L452R, T478K, D614G, P681R, and D950N.[1] Several of these mutations may affect immune responses directed toward the key antigenic regions of receptor-binding protein (452 and 478) and deletion of part of the N-terminal domain.[23] P681R is at the S1–S2 cleavage site, and it appears that strains with mutations at that site may have increased replication, which leads to higher viral loads and increased transmission.[24] Data on the effectiveness of Covid-19 vaccines against clinical outcomes with this variant have been limited. In this study, we aimed to estimate the effectiveness of two Covid-19 vaccines, BNT162b2 and ChAdOx1 nCoV-19 (AstraZeneca), against symptomatic disease caused by the delta variant.

METHODS

STUDY DESIGN

We used two approaches to estimate the effect of vaccination on the delta variant. First, we used a test-negative case–control design to estimate vaccine effectiveness against symptomatic disease caused by the delta variant, as compared with the alpha variant, over the period that the delta variant has been circulating. This approach has been described in detail elsewhere.[10] In brief, we compared vaccination status in persons with symptomatic Covid-19 with vaccination status in persons who reported symptoms but had a negative test. This approach helps to control for biases related to health-seeking behavior, access to testing, and case ascertainment.

For the secondary analysis, the proportion of persons with cases caused by the delta variant

relative to the main circulating virus (the alpha variant) was estimated according to vaccination status. The underlying assumption was that if the vaccine had some efficacy and was equally effective against each variant, a similar proportion of cases with either variant would be expected in unvaccinated persons and in vaccinated persons. Conversely, if the vaccine was less effective against the delta variant than against the alpha variant, then the delta variant would be expected to make up a higher proportion of cases occurring more than 3 weeks after vaccination than among unvaccinated persons. Details of this analysis are described in Section S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

DATA SOURCES

Vaccination Status

Data on all persons in England who have been vaccinated with Covid-19 vaccines are available in a national vaccination register (the National Immunisation Management System). Data regarding vaccinations that had occurred up to May 30, 2021, including the date of receipt of each dose of vaccine and the vaccine type, were extracted on June 1, 2021. Vaccination status was categorized as receipt of one dose of vaccine among persons who had symptom onset occurring 21 days or more after receipt of the first dose up to the day before the second dose was received, as receipt of the second dose among persons who had symptom onset occurring 14 days or more after receipt of the second dose, and as receipt of the first or second dose among persons with symptom onset occurring 21 days or more after the receipt of the first dose (including any period after the receipt of the second dose).

SARS-CoV-2 Testing

Polymerase-chain-reaction (PCR) testing for SARS-CoV-2 in the United Kingdom is undertaken by hospital and public health laboratories, as well as by community testing with the use of drive-through or at-home testing, which is available to anyone with symptoms consistent with Covid-19 (high temperature, new continuous cough, or loss or change in sense of smell or taste). Data on all positive PCR tests between October 26, 2020, and May 30, 2021, were extracted. Data on all recorded negative community tests among persons who reported symptoms were also extracted for the test-negative case–control analysis. Children younger than 16 years of age as of March 21, 2021, were excluded. Data were restricted to persons who had reported symptoms, and only persons who had undergone testing within 10 days after symptom onset were included, in order to account for reduced sensitivity of PCR testing beyond this period.[25]

Identification of Variant

Whole-genome sequencing was used to identify the delta and alpha variants. The proportion of all positive samples that were sequenced increased from approximately 10% in February 2021 to approximately 60% in May 2021.[4] Sequencing is undertaken at a network of laboratories, including the Wellcome Sanger Institute, where a high proportion of samples has been tested, and whole-genome sequences are assigned to Public Health England definitions of variants on the basis of mutations.[26]

Spike gene target status on PCR was used as a second approach for identifying each variant. Laboratories used the TaqPath assay (Thermo Fisher Scientific) to test for three gene targets: spike (*S*), nucleocapsid (*N*), and open reading frame 1ab (*ORF1ab*). In December 2020, the alpha variant was noted to be associated with negative testing on the *S* target, so *S* target–negative status was subsequently used as a proxy for identification of the variant. The alpha variant accounts for between 98% and 100% of *S* target–negative results in England. Among sequenced samples that tested positive for the *S* target, the delta variant was in 72.2% of the samples in April 2021 and in 93.0% in May (as of May 12, 2021).[4] For the test-negative case–control analysis, only samples that had been tested at laboratories with the use of the TaqPath assay were included.

Data Linkage

The three data sources described above were linked with the use of the National Health Service number (a unique identifier for each person receiving medical care in the United Kingdom). These data sources were also linked with data on the patient's date of birth, surname, first

name, postal code, and specimen identifiers and sample dates.

Covariates

Multiple covariates that may be associated with the likelihood of being offered or accepting a vaccine and the risk of exposure to Covid-19 or specifically to either of the variants analyzed were also extracted from the National Immunisation Management System and the testing data. These data included age (in 10-year age groups), sex, index of multiple deprivation (a national indication of level of deprivation that is based on small geographic areas of residence,[27] assessed in quintiles), race or ethnic group, care home residence status, history of foreign travel (i.e., outside the United Kingdom or Ireland), geographic region, period (calendar week), health and social care worker status, and status of being in a clinically extremely vulnerable group.[28] In addition, for the test-negative case–control analysis, history of SARS-CoV-2 infection before the start of the vaccination program was included. Persons were considered to have traveled if, at the point of requesting a test, they reported having traveled outside the United Kingdom and Ireland within the preceding 14 days or if they had been tested in a quarantine hotel or while quarantining at home. Postal codes were used to determine the index of multiple deprivation, and unique property-reference numbers were used to identify care homes.[29]

STATISTICAL ANALYSIS

For the test-negative case–control analysis, logistic regression was used to estimate the odds of having a symptomatic, PCR-confirmed case of Covid-19 among vaccinated persons as compared with unvaccinated persons (control). Cases were identified as having the delta variant by means of sequencing or if they were *S* target–positive on the TaqPath PCR assay. Cases were identified as having the alpha variant by means of sequencing or if they were *S* target–negative on the TaqPath PCR assay.

If a person had tested positive on multiple occasions within a 90-day period (which may represent a single illness episode), only the first positive test was included. A maximum of three randomly chosen negative test results were included for each person. Negative tests in which the sample had been obtained within 3 weeks before a positive result or after a positive result could have been false negatives; therefore, these were excluded. Tests that had been administered within 7 days after a previous negative result were also excluded. Persons who had previously tested positive before the analysis period were also excluded in order to estimate vaccine effectiveness in fully susceptible persons. All the covariates were included in the model as had been done with previous test-negative case–control analyses, with calendar week included as a factor and without an interaction with region.

With regard to *S* target–positive or –negative status, only persons who had tested positive on the other two PCR gene targets were included. Assignment to the delta variant on the basis of *S* target status was restricted to the week commencing April 12, 2021, and onward in order to aim for high specificity of *S* target–positive testing for the delta variant.[4]

Vaccine effectiveness for the first dose was estimated among persons with a symptom-onset date that was 21 days or more after receipt of the first dose of vaccine, and vaccine effects for the second dose were estimated among persons with a symptom-onset date that was 14 days or more after receipt of the second dose. Comparison was made with unvaccinated persons and with persons who had symptom onset in the period of 4 to 13 days after vaccination in order to help account for differences in underlying risk of infection. The period from the day of vaccine administration (day 0) to day 3 was excluded because reactogenicity to the vaccine can cause an increase in testing that biases results, as previously described.[10]

RESULTS

DATA LINKAGE

Among all the sequenced samples that were linked to the SARS-CoV-2 testing data set, 92.9% were linked to data on vaccination status. Over the course of the study period, there were 38,592 linked sequenced tests. In an analysis that was restricted to including only persons at least 16 years of age who had symptomatic Covid-19 caused by the alpha or delta variant and who had been vaccinated with either ChAdOx1 nCoV-19 or BNT162b2 according to an appropriate schedule, 19,109 sequenced cases were included (Fig. S1 in the Supplementary Appendix). The alpha

variant was detected in 14,837 samples, and the delta variant in 4272 samples.

DESCRIPTIVE CHARACTERISTICS

The characteristics of persons with Covid-19 in the study population according to variant are shown in Table 1. Key differences with the delta variant included a higher proportion of persons with a history of foreign travel; a higher proportion of persons with cases in the most recent weeks (calendar weeks 18 to 20); a higher proportion of persons with cases in the northwest region, London, and the east of England; and a higher proportion of persons in the "Indian or British Indian," "Pakistani or British Pakistani," or "any other Asian background" ethnic groups. Little difference in the distribution of age or index of multiple deprivation was seen. Few cases of either variant were seen in persons older than 70 years of age, and only nine cases (all of which were with the alpha variant) occurred among care home residents.

Among sequenced samples that were originally tested with the use of the TaqPath assay, a high correlation was seen between S target status and the two variants under investigation, with 95.3% of the S target–positive cases identified as having the delta variant and 99.6% of the S target–negative cases identified as having the alpha variant (Tables S1 and S2). The distribution of intervals between the receipt of vaccine doses is shown in Figure S2.

VACCINE EFFECTIVENESS ESTIMATES

Results of the test-negative case–control analysis are shown in Table 2 and Figure 1. In the "any vaccine" analysis, in which data from the persons who received either vaccine were pooled, effectiveness was notably lower after the first vaccine dose among persons with the delta variant (30.7%; 95% confidence interval [CI], 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7). Results for the first dose were similar for both vaccines, with an absolute difference in vaccine effectiveness against the delta variant as compared with the alpha variant of 11.9 percentage points with the BNT162b2 vaccine and 18.7 percentage points with the ChAdOx1 nCoV-19 vaccine.

The difference in vaccine effectiveness was much smaller among persons who had received the second dose of vaccine. In the "any vaccine" analysis, the vaccine effectiveness was 87.5% (95% CI, 85.1 to 89.5) with the alpha variant and 79.6% (95% CI, 76.7 to 82.1) with the delta variant. With the BNT162b2 vaccine, a small difference in effectiveness between variants was seen after the second dose: 93.7% (95% CI, 91.6 to 95.3) with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) with the delta variant. The effectiveness with two doses of the ChAdOx1 nCoV-19 vaccine was lower than with the BNT162b2 vaccine; however, with the ChAdOx1 nCoV-19 vaccine, the difference in effectiveness between the alpha and delta variants was small (74.5% [95% CI, 68.4 to 79.4] and 67.0% [95% CI, 61.3 to 71.8], respectively).

Table S3, in which the period after the first dose is stratified according to the period of 21 to 55 days and the period of 56 or more days, shows a possible indication of waning efficacy against the alpha variant with the BNT162b2 vaccine and against the delta variant with the ChAdOx1 nCoV-19 vaccine. Section S1 and Tables S4 through S6 show the results of the secondary analysis.

DISCUSSION

We found that the absolute difference in vaccine effectiveness against symptomatic disease with one dose of vaccine with the delta variant as compared with the alpha variant was approximately 12 to 19 percentage points. However, the differences in vaccine effectiveness after two doses were small. This was the case for both the BNT162b2 and ChAdOx1 nCoV-19 vaccines. In the test-negative case–control analysis, the estimated vaccine effectiveness against symptomatic disease with the delta variant was approximately 36% with a single dose of the BNT162b2 vaccine and approximately 30% with a single dose of the ChAdOx1 nCoV-19 vaccine; the effectiveness was approximately 88% with two doses of the BNT162b2 vaccine and approximately 67% with two doses of the ChAdOx1 nCoV-19 vaccine.

A clear effect was noted with both vaccines, with high levels of effectiveness after two doses. Vaccine effectiveness against either variant was smaller after the receipt of two doses of the ChAdOx1 nCoV-19 vaccine than after the receipt of two doses of the BNT162b2 vaccine, a finding that is consistent with reported clinical trial findings.[7,8] Differences between the two vaccines

Table 1. Characteristics of Persons with Covid-19 in the United Kingdom, According to Variant.*

Characteristic	Alpha Variant (N=14,837)	Delta Variant (N=4272)	Total (N=19,109)
Percent of total cases	77.6	22.4	100
Age — no. (%)			
16–29 yr	5,325 (35.9)	1571 (36.8)	6,896 (36.1)
30–39 yr	4,199 (28.3)	1164 (27.2)	5,363 (28.1)
40–49 yr	2,923 (19.7)	834 (19.5)	3,757 (19.7)
50–59 yr	1,532 (10.3)	465 (10.9)	1,997 (10.5)
60–69 yr	657 (4.4)	178 (4.2)	835 (4.4)
70–79 yr	163 (1.1)	47 (1.1)	210 (1.1)
≥80 yr	38 (0.3)	13 (0.3)	51 (0.3)
History of travel — no. (%)†			
No	14,689 (99.0)	4219 (98.8)	18,908 (98.9)
Yes	100 (0.7)	52 (1.2)	152 (0.8)
Unknown	48 (0.3)	1 (<0.1)	49 (0.3)
Week that sample was obtained — no. (%)‡			
14	3,316 (22.3)	19 (0.4)	3,335 (17.5)
15	2,780 (18.7)	53 (1.2)	2,833 (14.8)
16	2,517 (17.0)	184 (4.3)	2,701 (14.1)
17	2,156 (14.5)	372 (8.7)	2,528 (13.2)
18	1,775 (12.0)	737 (17.3)	2,512 (13.1)
19	1,263 (8.5)	1111 (26.0)	2,374 (12.4)
20	1,030 (6.9)	1796 (42.0)	2,826 (14.8)
Week of symptom onset — no. (%)‡			
12	28 (0.2)	0	28 (0.1)
13	1,431 (9.6)	8 (0.2)	1,439 (7.5)
14	3,089 (20.8)	26 (0.6)	3,115 (16.3)
15	2,547 (17.2)	89 (2.1)	2,636 (13.8)
16	2,381 (16.0)	230 (5.4)	2,611 (13.7)
17	1,965 (13.2)	501 (11.7)	2,466 (12.9)
18	1,622 (10.9)	917 (21.5)	2,539 (13.3)
19	1,178 (7.9)	1311 (30.7)	2,489 (13.0)
20	596 (4.0)	1190 (27.9)	1,786 (9.3)
Sex — no. (%)			
Female	7,681 (51.8)	2047 (47.9)	9,728 (50.9)
Male	7,151 (48.2)	2222 (52.0)	9,373 (49.1)
Missing data	5 (<0.1)	3 (0.1)	8 (<0.1)
Index of multiple deprivation — no. (%)§			
1	4,780 (32.2)	1446 (33.8)	6,226 (32.6)
2	3,302 (22.3)	950 (22.2)	4,252 (22.3)
3	2,592 (17.5)	654 (15.3)	3,246 (17.0)
4	2,302 (15.5)	687 (16.1)	2,989 (15.6)

Table 1. (Continued.)

Characteristic	Alpha Variant (N=14,837)	Delta Variant (N=4272)	Total (N=19,109)
5	1,828 (12.3)	524 (12.3)	2,352 (12.3)
Missing data	33 (0.2)	11 (0.3)	44 (0.2)
Clinically extremely vulnerable group — no. (%)¶			
No	14,582 (98.3)	4211 (98.6)	18,793 (98.3)
Yes	255 (1.7)	61 (1.4)	316 (1.7)
Care home resident — no. (%)			
No	14,828 (99.9)	4272 (100)	19,100 (100)
Yes	9 (0.1)	0	9 (<0.1)
Health or social care worker — no. (%)			
No	14,621 (98.5)	4181 (97.9)	18,802 (98.4)
Yes	216 (1.5)	91 (2.1)	307 (1.6)
Race or ethnic group — no. (%)‖			
Bangladeshi or British Bangladeshi	230 (1.6)	98 (2.3)	328 (1.7)
Chinese	54 (0.4)	18 (0.4)	72 (0.4)
Indian or British Indian	458 (3.1)	705 (16.5)	1,163 (6.1)
Pakistani or British Pakistani	1,024 (6.9)	510 (11.9)	1,534 (8.0)
Any other Asian background	278 (1.9)	188 (4.4)	466 (2.4)
Black African or Caribbean	277 (1.9)	113 (2.6)	390 (2.0)
White	9,662 (65.1)	1801 (42.2)	11,463 (60.0)
Mixed	234 (1.6)	71 (1.7)	305 (1.6)
Any other ethnic group	442 (3.0)	139 (3.3)	581 (3.0)
Missing data	2,178 (14.7)	629 (14.7)	2,807 (14.7)
Region — no. (%)			
East Midlands	1,822 (12.3)	380 (8.9)	2,202 (11.5)
East of England	1,178 (7.9)	510 (11.9)	1,688 (8.8)
London	1,062 (7.2)	536 (12.5)	1,598 (8.4)
Northeast	977 (6.6)	69 (1.6)	1046 (5.5)
Northwest	2,664 (18.0)	2138 (50.0)	4,802 (25.1)
Southeast	847 (5.7)	198 (4.6)	1045 (5.5)
Southwest	198 (1.3)	63 (1.5)	261 (1.4)
West Midlands	1,538 (10.4)	241 (5.6)	1,779 (9.3)
Yorkshire and Humber	4,550 (30.7)	135 (3.2)	4,685 (24.5)
Missing data	1 (<0.1)	2 (<0.1)	3 (<0.1)

* B.1.1.7 is the alpha variant, and B.1.617.2 the delta variant, of the severe acute respiratory syndrome coronavirus 2, the virus that causes coronavirus disease 2019 (Covid-19). Percentages may not total 100 because of rounding.
† Persons were considered to have traveled if, at the point of requesting a test, they reported having traveled outside the United Kingdom and Ireland within the preceding 14 days or if they had been tested in a quarantine hotel or while quarantining at home.
‡ The week number is the calendar week in 2021.
§ The index of multiple deprivation is a national indicator of level of deprivation on the basis of small geographic areas of residence; the index ranges from 1 (least deprived) to 5 (most deprived).[27]
¶ The status of being in a clinically extremely vulnerable group was defined according to NHS Digital.[28]
‖ Race or ethnic group was determined from data in the National Immunisation Management System register.

Table 2. Vaccine Effectiveness against the Alpha Variant or *S* Target–Negative Status and the Delta Variant or *S* Target–Positive Status, According to Dose and Vaccine Type.*

Vaccination Status	Test-Negative Status	Alpha Variant or *S* Target–Negative Status			Delta Variant or *S* Target–Positive Status		
	Controls	Cases	Case:Control Ratio	Adjusted Vaccine Effectiveness (95% CI)	Cases	Case:Control Ratio	Adjusted Vaccine Effectiveness (95% CI)
	no.	*no.*		%	*no.*		%
Unvaccinated	96,371	7313	0.076	Reference	4043	0.042	Reference
Any vaccine							
Dose 1	51,470	2226	0.043	48.7 (45.5–51.7)	1493	0.029	30.7 (25.2–35.7)
Dose 2	23,993	143	0.006	87.5 (85.1–89.5)	340	0.014	79.6 (76.7–82.1)
BNT162b2 vaccine							
Dose 1	8,641	450	0.052	47.5 (41.6–52.8)	137	0.016	35.6 (22.7–46.4)
Dose 2	15,749	49	0.003	93.7 (91.6–95.3)	122	0.008	88.0 (85.3–90.1)
ChAdOx1 nCoV-19 vaccine							
Dose 1	42,829	1776	0.041	48.7 (45.2–51.9)	1356	0.032	30.0 (24.3–35.3)
Dose 2	8,244	94	0.011	74.5 (68.4–79.4)	218	0.026	67.0 (61.3–71.8)

* The adjusted analysis of vaccine effectiveness was adjusted for period (calendar week), travel history, race or ethnic group, sex, age, index of multiple deprivation, clinically extremely vulnerable group, region, history of positive test, health or social care worker, and care home residence. CI denotes confidence interval.

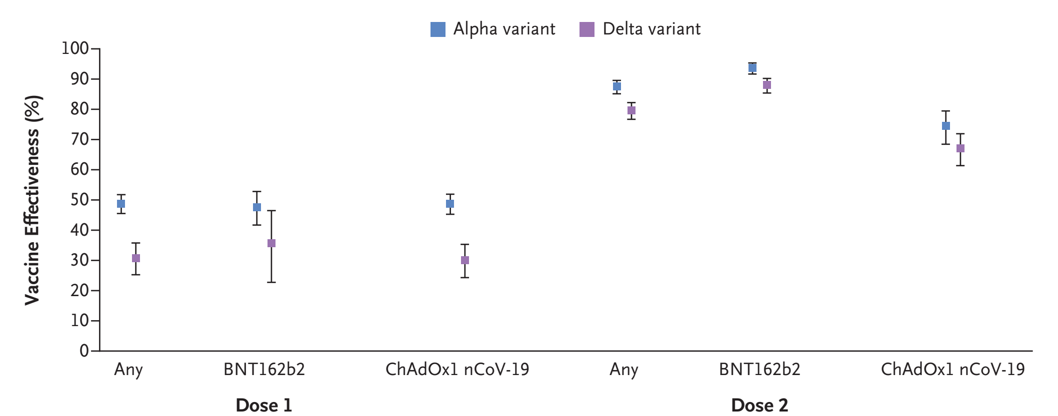

Figure 1. Vaccine Effectiveness against the Alpha and Delta Variants, According to Dose and Vaccine Type.
Shown is the effectiveness of one dose and two doses of the BNT162b2 and ChAdOx1 nCoV-19 vaccines, or either vaccine ("any"), against symptomatic disease with the B.1.1.7 (alpha) or B.1.617.2 (delta) variant of the severe acute respiratory syndrome coronavirus 2. I bars indicate 95% confidence intervals.

are further discussed in Section S2. The numbers of cases and follow-up periods are currently insufficient for the estimation of vaccine effectiveness against severe disease, including hospitalization and death.

One study from India that reported neutralization data in the broader B.1.617 variant category suggested that convalescent serum samples from persons with Covid-19 and from recipients of the BBV152 vaccine (Covaxin) were able to

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neutralize variants in the B.1.617 lineage.[30] As compared with recent findings from Qatar on the effectiveness of the BNT162b2 vaccine against the alpha and beta variants,[17] our findings suggest that effectiveness against the delta variant after a full vaccination course lies somewhere between these two. A comparison with previously reported estimates of vaccine effectiveness against the alpha variant is discussed in Section S2.

The large scale of testing and whole-genome sequencing in the United Kingdom, as well as the recording of vaccination status in a national vaccination register, allowed us to analyze vaccine effectiveness within a few weeks of the delta variant first emerging in the United Kingdom. We used two distinct analytic approaches that gave broadly similar results, and findings with our control analysis (using the alpha variant) are consistent with those that have been reported previously.[7,8,10,17] Findings were also similar to those in cases that occurred during the first 2 weeks after receipt of the first vaccine dose (Table S4), which helps to rule out unmeasured confounders associated with both the likelihood of being vaccinated and the likelihood of being exposed to a variant. The use of a test-negative case–control design helped us to control for differences in health-seeking behavior between vaccinated persons and unvaccinated persons.

Our study has several limitations. The findings are observational and should be interpreted with caution. Low sensitivity or specificity of PCR testing could result in cases and controls being misclassified, which would attenuate the estimates of vaccine effectiveness. Low sensitivity or specificity of PCR testing could also affect one variant more than another, although this might be expected to affect the alpha variant more than the delta variant, given that, with an emerging variant, more cases may be detected earlier in infection, which may result in higher viral loads and increased sensitivity and specificity. Although we controlled for race or ethnic group, region, and an index of multiple deprivation, differences in vaccine coverage among population groups that may have more or less exposure to the delta variant may have affected the secondary analysis but should not have affected the test-negative case–control design. There may also be differences among the populations that received each vaccine — for example, in younger age groups, health care workers are more likely to have received the BNT162b2 vaccine, whereas persons in clinical risk groups are more likely to have received the ChAdOx1 nCoV-19 vaccine.[11] Furthermore, the analysis also relied on the assumptions that any residual confounding in the test-negative case–control design would affect the two estimates of vaccine effectiveness equally or at least would not bias the adjusted odds ratio for the comparison of vaccine effectiveness for a given vaccine against the two variants; that is, the accuracy of the sequencing would not depend on the variant and the propensity among symptomatic persons to get tested would not differ according to variant.

Overall, we found high levels of vaccine effectiveness against symptomatic disease with the delta variant after the receipt of two doses. These estimates were only modestly lower than the estimate of vaccine effectiveness against the alpha variant. Our finding of reduced effectiveness after the first dose would support efforts to maximize vaccine uptake with two doses among vulnerable groups in the context of circulation of the delta variant.

Surveillance of coronavirus disease 2019 (Covid-19) testing and vaccination is undertaken under Regulation 3 of the Health Service (Control of Patient Information) Regulations 2002 to collect confidential patient information (www.legislation.gov.uk/uksi/2002/1438/regulation/3/made) under Sections 3(i) (a) to (c), 3(i)(d) (i) and (ii), and 3. The study protocol was subject to an internal review by the Public Health England Research Ethics and Governance Group and was found to be fully compliant with all regulatory requirements. Given that no regulatory issues were identified and that ethics review is not a requirement for this type of work, it was decided that a full ethics review would not be necessary.

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On August 24, 2021, this report was posted online as an MMWR *Early Release.*

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During December 14, 2020–April 10, 2021, data from the HEROES-RECOVER Cohorts,* a network of prospective cohorts among frontline workers, showed that the Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines were approximately 90% effective in preventing symptomatic and asymptomatic infection with SARS-CoV-2, the virus that causes COVID-19, in real-world conditions (*1*,*2*). This report updates vaccine effectiveness (VE) estimates including all COVID-19 vaccines available through August 14, 2021, and examines whether VE differs for adults with increasing time since completion of all recommended vaccine doses. VE before and during SARS-CoV-2 B.1.617.2 (Delta) variant predominance, which coincided with an increase in reported COVID-19 vaccine breakthrough infections, were compared (*3*,*4*).

Methods for the HEROES-RECOVER Cohorts have been published previously (*1*,*2*,*5*). Health care personnel, first responders, and other essential and frontline workers in eight U.S. locations across six states were tested weekly for SARS-CoV-2 infection by reverse transcription–polymerase chain reaction (RT-PCR)[†] and upon the onset of any COVID-19–like illness. Weeks when the Delta variant accounted for ≥50% of viruses sequenced, based on data from each respective location, were defined as weeks of Delta variant predominance. Vaccination was documented by self-report and verified by provision of vaccine cards or extraction from electronic medical records or state immunization registries. Among 4,217 participants, 3,483 (83%) were vaccinated; 2,278 (65%) received Pfizer-BioNTech, 1,138 (33%) Moderna, and 67 (2%) Janssen (Johnson & Johnson) COVID-19 vaccines. Cox proportional hazards models were used to calculate ratios of unvaccinated to fully vaccinated (≥14 days after receipt of all recommended COVID-19 vaccine doses) infection rates, adjusted for occupation, site, and local viral circulation (*6*), and weighted for inverse probability of vaccination using sociodemographic characteristics, health information, frequency of close social contact, and mask use. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§]

During the 35-week study period, 4,136 participants with no previous laboratory-documented SARS-CoV-2 infection contributed a median of 20 unvaccinated days per participant (interquartile range [IQR] = 8–45 days; total = 181,357 days), during which 194 SARS-CoV-2 infections were identified; 89.7% of these infections were symptomatic. A total of 2,976 participants contributed a median of 177 fully vaccinated days (IQR = 115–195 days; total = 455,175 days) with 34 infections, 80.6% of which were symptomatic. Adjusted VE against SARS-CoV-2 infection was 80% (95% confidence interval [CI] = 69%–88%). The VE point estimate was 85% among participants for whom <120 days had elapsed since completion of full vaccination compared with 73% among those for whom ≥150 days had elapsed; however the VE 95% CI were overlapping, indicating the difference was not statistically significant (Table).

During Delta variant–predominant weeks at study sites, 488 unvaccinated participants contributed a median of 43 days (IQR = 37–69 days; total = 24,871 days) with 19 SARS-CoV-2 infections (94.7% symptomatic); 2,352 fully vaccinated participants contributed a median of 49 days (IQR = 35–56 days; total = 119,218 days) with 24 SARS-CoV-2 infections (75.0% symptomatic). Adjusted VE during this Delta predominant period was 66% (95% CI = 26%–84%) compared with 91% (95% CI = 81%–96%) during the months preceding Delta predominance.

During December 14, 2020–August 14, 2021, full vaccination with COVID-19 vaccines was 80% effective in preventing RT-PCR–confirmed SARS-CoV-2 infection among frontline workers, further affirming the highly protective benefit of full vaccination up to and through the most recent summer U.S. COVID-19 pandemic waves. The VE point estimates declined from 91% before predominance of the SARS-CoV-2 Delta variant to 66% since the SARS-CoV-2 Delta variant became predominant at the HEROES-RECOVER cohort study sites; however, this trend should be interpreted with caution because VE might also be declining as time since vaccination increases and because of poor precision in estimates due to limited number of weeks of observation and few infections among participants. As with all observational VE studies, unmeasured and residual confounding might be present. Active surveillance through the cohort is ongoing and VE estimates will be monitored continuously. Although these interim findings suggest a moderate reduction in the effectiveness of COVID-19 vaccines in preventing infection, the sustained two thirds reduction in infection risk underscores the continued importance and benefits of COVID-19 vaccination.

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* Arizona Healthcare, Emergency Response and Other Essential Workers Surveillance Study (HEROES) conducted in Phoenix, Tucson, and other noncentrally located areas in Arizona; Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) conducted in Miami, Florida; Duluth, Minnesota; Portland, Oregon; Temple, Texas; and Salt Lake City, Utah.

† RT-PCR was conducted using the Quidel Lyra SARS-CoV-2 Assay (before November 2020) or TaqPath COVID-19 Combo Kit (Applied Biosystems) at the Marshfield Clinic Research Institute (Marshfield, WI).

§ 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect 241(d); 5 U.S.C. Sect 552a; 44 U.S.C. Sect 3501 et seq.

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TABLE. Effectiveness of COVID-19 vaccines against any SARS-CoV-2 infection among frontline workers, by B.1.617.2 (Delta) variant predominance and time since full vaccination — eight U.S. locations, December 2020–August 2021

Period and vaccination status	No. of contributing participants*	Total no. of person-days	Median days (IQR)	No. of SARS-CoV-2 infections	Adjusted VE,† % (95% CI)
Full cohort to date					
Unvaccinated	4,136	181,357	20 (8–45)	194	N/A
Fully vaccinated§	2,976	454,832	177 (115–195)	34	80 (69–88)
14–119 days after full vaccination	2,923	284,617	106 (106–106)	13	85 (68–93)

Period and vaccination status	No. of contributing participants*	Total no. of person-days	Median days (IQR)	No. of SARS-CoV-2 infections	Adjusted VE,† % (95% CI)
120–149 days after full vaccination	2,369	66,006	30 (30–30)	3	81 (34–95)
≥150 days after full vaccination	2,129	104,174	52 (37–64)	18	73 (49–86)
Pre-Delta variant predominance					
Unvaccinated	4,137	156,626	19 (8–43)	175	N/A
Fully vaccinated	2,875	329,865	124 (95–149)	10	91 (81–96)
Delta variant predominance					
Unvaccinated	488	24,871	43 (37–69)	19	N/A
Fully vaccinated	2,352	119,218	49 (35–56)	24	66 (26–84)

Abbreviations: CI = confidence interval; IQR = interquartile range; N/A = not applicable; SMD = standardized mean difference; VE = vaccine effectiveness.

* Person-days between the date of any dose of COVID-19 vaccine and fully vaccinated status were excluded from VE models because of indeterminate immune status. Participants with SARS-CoV-2 infection during this period were also excluded; in the pre-Delta period, 47 participants were excluded, and in the Delta period, two participants were excluded. Contributing participants in vaccination categories also do not equal the total number of participants in the cohort.

† Adjusted VE was inversely weighted for probability of being vaccinated and adjusted for local virus circulation, study location, and occupation. Delta variant models were additionally adjusted for ethnicity. All Cox regression models met the proportional hazards assumption. To calculate the probability of being vaccinated for each period, boosted regression models were fit including covariates for site, sociodemographic characteristics, health information, frequency of close social contact, mask use, and local virus circulation. In the full cohort to date and the pre-Delta cohort, all covariates met balance criteria of SMD<0.2 after weighting except mask use at work (SMD = 0.227 and 0.207, respectively) but was not found to change VE estimates by ≥3% when added to the models. In the Delta predominant cohort occupation, ethnicity, influenza vaccination, and mask use at work did not meet balance criteria (SMD range = 0.206–0.288); influenza vaccination and mask use at work did not change VE estimates by ≥3%; however, occupation and ethnicity did change VE by ≥3% and were therefore included as covariates in the Cox regression model for VE.

§ Fully vaccinated was defined as ≥14 days after receipt of all recommended COVID-19 vaccine doses.

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Research

BMJ

Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial

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Abstract

Objective To determine whether vaccination of care home staff against influenza indirectly protects residents.
Design Pair matched cluster randomised controlled trial.
Setting Large private chain of UK care homes during the winters of 2003-4 and 2004-5.
Participants Nursing home staff (n = 1703) and residents (n = 2604) in 44 care homes (22 intervention homes and 22 matched control homes).
Interventions Vaccination offered to staff in intervention homes but not in control homes.
Main outcome measures The primary outcome was all cause mortality of residents. Secondary outcomes were influenza-like illness and health service use in residents.
Results In 2003-4 vaccine coverage in full time staff was 48.2% (407/884) in intervention homes and 5.9% (51/859) in control homes. In 2004-5 uptake rates were 43.2% (365/844) and 3.5% (28/800). National influenza rates were substantially below average in 2004-5. In the 2003-4 period of influenza activity significant decreases were found in mortality of residents in intervention homes compared with control homes (rate difference −5.0 per 100 residents, 95% confidence interval −7.0 to −2.0) and in influenza-like illness (P = 0.004), consultations with general practitioners for influenza-like illness (P = 0.008), and admissions to hospital with influenza-like illness (P = 0.009). No significant differences were found in 2004-5 or during periods of no influenza activity in 2003-4.
Conclusions Vaccinating care home staff against influenza can prevent deaths, health service use, and influenza-like illness in residents during periods of moderate influenza activity.
Trial registration National Research Register N0530147256.

Introduction

Influenza is an important cause of mortality, morbidity, and health service use in elderly patients.[1] The virus can spread particularly rapidly in care homes,[2] with attack rates ranging from 20-40%[3–7] but potentially reaching 60% of residents.[8] Complications are common, with admission rates to hospital often exceeding 10%[4–6 8] and case fatality rates often exceeding 5%[4–8] and reaching 55%.[3] Vaccination of care home residents against influenza is effective in preventing respiratory illness, admissions to hospital, and death.[9–11] The immune response to influenza vaccine in elderly patients (especially those with comorbidities) is, however, reduced, so that protection is only 50-70%.[12 13] Residents are therefore vulnerable to influenza outbreaks even when vaccination coverage is high.[3–5 7]

In many countries it is recommended that acute hospitals offer influenza vaccine to healthcare workers annually.[14] Employers in the United Kingdom are advised to consider providing vaccination for care home staff, but most do not.[15] Evidence shows that vaccination of healthcare workers can reduce serologically confirmed influenza by nearly 90% in those vaccinated.[16] An indirect effect may also exist whereby immune staff do not infect patients.[17 18] Two previous cluster randomised controlled trials showed that influenza vaccination of healthcare workers on wards for the care of elderly people in Scotland led to a decrease in mortality among patients.[17 18] Results have been questioned owing to the relatively small number of wards randomised (which led to unbalanced randomisation) and because it was not possible to show that the reductions in mortality were related temporally to influenza activity on the wards or in the community.[19] We studied the effect of vaccinating care home staff against influenza on mortality, health service use, and influenza-like illness among residents. To overcome some of the methodological limitations of previous studies we randomised a large number of units and balanced these on baseline characteristics. We used cluster randomisation to look for indirect effects of vaccination and because the intervention was best applied at the level of the care home.[20] We compared the effectiveness of the intervention during periods with differing levels of influenza activity in the community as this is likely to influence the effect size. The study is reported according to the guidelines of the consolidated standards of reporting trials for cluster randomised controlled trials.[21]

Methods

We carried out a pair matched cluster randomised controlled trial of promotion and delivery of influenza vaccine to care home staff over the winters of 2003-4 and 2004-5, with collection of aggregate data on outcomes among residents. The study was carried out in a large private chain of UK care homes. Residents were predominantly elderly and required a mixture of nursing and residential care. The company's policy (in common with most UK care homes) was not to offer staff influenza vaccination. The homes routinely offer influenza vaccine to all residents and

P+ *Forest plots for rate differences during year 1 are on bmj.com*

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arrange this through local general practitioners. We excluded homes in Scotland and Wales for logistical reasons.

Intervention

For the purposes of the study the company agreed to adopt a policy for influenza vaccination of staff in randomly selected intervention homes while maintaining their usual policy of not actively promoting staff vaccination in control homes. Lead nurses in each of the intervention homes were trained to promote influenza vaccine to staff. They were encouraged to act as advocates for vaccination and to use word of mouth, leaflets, and posters to promote vaccination. Staff in intervention homes were eligible for vaccination and were sent a letter explaining the study and the potential benefits of influenza vaccination. The lead nurse liaised with a local occupational health service to arrange for three vaccination sessions within the homes in October, including at least one session during a night shift to maximise uptake. Staff in control homes were sent a letter informing them of the study and advising them of the Department of Health recommendation that adults with chronic illness should be vaccinated by their general practitioner. We did not seek to influence vaccination of residents.

We hypothesised that the vaccine promotion programme for staff would reduce transmission of influenza to residents and therefore reduce influenza-like illness and associated deaths and health service use in residents during and immediately after periods of influenza virus activity but not at other times.

Outcomes

Outcomes were measured in residents and collected as aggregate data within each home. The primary outcome was all cause mortality of residents. Secondary outcomes were influenza-like illness, mortality with influenza-like illness, admissions to hospital from any cause, admissions to hospital with influenza-like illness, and consultations with a general practitioner for influenza-like illness. The lead nurses at each home were trained to collect daily data about the numbers of residents at the home and the numbers who experienced primary or secondary outcomes. Influenza-like illness was defined as a fever of 37.8°C or more (measured orally), or an acute deterioration in physical or mental ability, plus either new onset of one or more respiratory symptoms or an acute worsening of a chronic condition involving respiratory symptoms. This case definition was adapted from others used in this setting.[4-7] Since elderly people often do not have a fever, our definition did not require a raised temperature. Data were returned weekly. Data collection took place from 3 November 2003 to 28 March 2004 and from 1 November 2004 to 27 March 2005. Only aggregate nonidentifiable data were collected.

Sample size and randomisation

Sample size calculations for cluster randomised controlled trials[22] were applied to data from a pilot study and previous studies.[17 18] To detect a reduction in all cause mortality from 15% to 10% (intracluster variance 2.3%) with 90% power at the 5% significance level we determined that we required 20 pairs of homes, with an average of 50 residents each, studied for one winter. The study was carried out over two consecutive years to minimise the possibility of negative results because of low influenza activity.

For all homes we obtained data on the number of residents, the proportion requiring high dependency care, and mortality. We placed homes into matched pairs within three regions (northern, central, and southern England) on the basis of the following order of priority: size of home, percentage of high dependency, and mortality of residents. We then selected the 25 most closely matching pairs of homes. A researcher blinded to the home's identity and characteristics carried out randomisation within these pairs using random number tables.

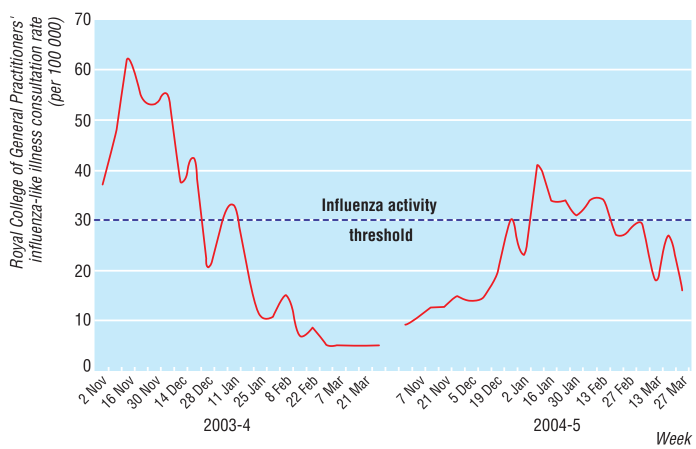

Fig 1 Royal College of General Practitioners' consultation rate for influenza-like illness (consultations per 100 000 population) and periods of influenza activity

Statistical analysis

We used national data from the Royal College of General Practitioners' sentinel surveillance scheme to divide the study into periods of influenza activity and no activity.[23] The start of the period of influenza activity was defined as the beginning of the week in which the weekly consultation rate rose above 30 per 100 000 (standard cut-off point for defining normal seasonal influenza activity). The end was defined as one week after the weekly consultation rate returned and remained below this baseline level for influenza-like illness and for general practitioner consultations for influenza-like illness, and two weeks after the consultation rate fell below baseline for admissions to hospital and deaths, thus taking into account a plausible timescale for development and progression of disease (fig 1).

We analysed outcomes at a cluster level rather than individual level using aggregate data for each cluster. To take account of the matched clustered design we used a random effects meta-analysis.[24] This treated the results from each pair of homes as a separate study and provided a pooled estimate of effect weighted for the size of homes and the size of the effects and their standard errors. We calculated the outcome rates per resident period for each home during periods of influenza activity and no activity. The rates were measures based on person time where the denominator was the average number of residents during the period of interest (calculated as the number of occupied bed days during the period divided by the number of days in the period) and the numerator was the number of events in these residents during the period. For each pair of homes we calculated the rate difference (intervention minus control); a negative rate difference indicating that the intervention prevented events. We used RevMan software to produce forest plots of rate differences for each pair of homes and weighted estimates of the overall rate difference, 95% confidence intervals, and levels of statistical significance. To test for interaction between year and intervention we used a multilevel Poisson model.

When significant protection of residents was observed we calculated the number of staff vaccinations needed to prevent one event in residents (number needed to treat) as number of

Table 1 Baseline characteristics of residents in intervention and control homes

Characteristic	Intervention homes		Control homes	
	2003-4	2004-5	2003-4	2004-5
No of residents	1233	1270	1371	1391
Mean age (years)	83.0	82.7	82.6	83.0
No (%) of women	866 (70.2)	897 (70.6)	972 (70.9)	976 (70.2)
No (%) highly dependent*	444 (36.0)	627 (49.4)	568 (41.4)	640 (46.0)
No (%) vaccinated	964 (78.2)	895 (70.5)	979 (71.4)	989 (71.1)

*Classified according to nursing home chain's in-house scoring system. Patients classed as highly dependent (for example, bedridden or severely demented patients) required more intensive care.

vaccinations given in all intervention homes divided by the average number of residents in all intervention homes multiplied by the weighted rate difference.

Results

Figure 1 shows the Royal College of General Practitioners' consultation rate for 2003-4 and 2004-5 and our periods of influenza activity for influenza-like illness and general practitioner consultations for influenza-like illness, admissions to hospital, and deaths. According to surveillance, influenza activity was below average in 2003-4 but nearly double that in 2004-5.[23] In both years laboratory surveillance confirmed that influenza A H3N2 was circulating during these periods (Fujian subtype in 2003-4 and Wellington subtype in 2004-5).

One care home withdrew after randomisation, and two were unable to provide regular data on outcomes. These homes and their matching homes were excluded, leaving 22 pairs (fig 2). Analyses relate to these 22 pairs (no outcome data were available for the excluded homes so an intention to treat analysis was not possible). No significant differences were found between baseline characteristics of the excluded pairs and the remaining homes. Influenza vaccine coverage among full time staff in intervention homes was 48.2% in 2003-4 and 43.2% in 2004-5 compared with 5.9% and 3.5% in control homes. This includes a small number of staff in intervention and control homes who were vaccinated by their general practitioner or through a different occupational health service. Uptake was lower in part time staff: 21.2% and 18.4% in intervention homes and 4.0% and 4.0% in control homes. In both years the influenza A H3N2 subtype included in

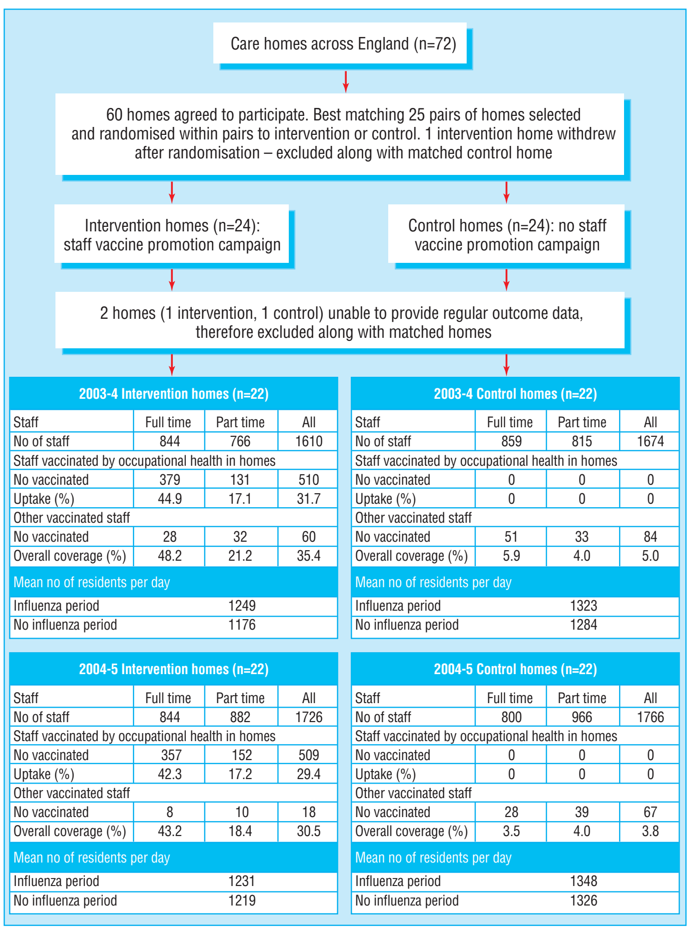

Fig 2 Participant flow

Table 2 Numbers of outcome events and event rates in intervention and control homes

	Intervention homes		Control homes		Weighted rate difference (95% CI)	P value
	No of events	Events per resident	No of events	Events per resident		
Year 1						
Period of influenza activity:						
No of residents	n=1249*		n=1323*		—	—
Death	140	0.112	203	0.153	−0.05 (−0.07 to −0.02)	0.002
Influenza-like illness	142	0.114	300	0.227	−0.09 (−0.14 to −0.03)	0.004
General practitioner consultations for influenza-like illness	125	0.100	247	0.187	−0.07 (−0.12 to −0.02)	0.002
Admissions to hospital	105	0.084	144	0.109	−0.02 (−0.05 to 0.02)	0.35
Admissions with influenza-like illness	4	0.003	23	0.017	−0.02 (−0.03 to 0.00)	0.009
Death with influenza-like illness	13	0.010	19	0.014	−0.01 (−0.02 to 0.01)	0.24
Period of no activity:						
No of residents	n=1176*		n=1284*		—	—
Death	97	0.082	94	0.073	0.00 (−0.03 to 0.03)	0.93
Influenza-like illness	114	0.097	114	0.089	0.00 (−0.05 to 0.05)	0.93
General practitioner consultations for influenza-like illness	87	0.074	99	0.077	−0.01 (−0.06 to 0.041)	0.74
Admissions to hospital	77	0.065	86	0.067	0.00 (−0.04 to 0.03)	0.80
Admissions with influenza-like illness	3	0.003	8	0.006	−0.01 (−0.02 to 0.01)	0.32
Death with influenza-like illness	6	0.005	7	0.005	−0.01 (−0.04 to 0.02)	0.59
Year 2						
Period of influenza activity:						
No of residents	n=1231*		n=1348*		—	—
Death	99	0.080	123	0.091	−0.01 (−0.04 to 0.02)	0.49
Influenza-like illness	149	0.121	179	0.133	0.00 (−0.06 to 0.06)	0.93
General practitioner consultations for influenza-like illness	124	0.101	155	0.115	−0.01 (−0.07 to 0.05)	0.77
Admissions to hospital	93	0.076	102	0.076	−0.00 (−0.03 to 0.04)	0.84
Admissions with influenza-like illness	12	0.010	9	0.007	0.00 (−0.02 to 0.02)	0.99
Death with influenza-like illness	4	0.003	14	0.010	−0.01 (−0.03 to 0.00)	0.08
Period of no activity:						
No of residents	n=1219*		n=1326*		—	—
Death	165	0.135	159	0.120	0.01 (−0.03 to 0.04)	0.70
Influenza-like illness	247	0.203	243	0.183	0.03 (−0.07 to 0.12)	0.57
General practitioner consultations for influenza-like illness	177	0.145	211	0.159	0.00 (−0.08 to 0.08)	0.95
Admissions to hospital	123	0.101	134	0.101	0.00 (−0.03 to 0.03)	0.86
Admissions with influenza-like illness	12	0.010	8	0.006	0.01 (0.00 to 0.02)	0.31
Death with influenza-like illness	12	0.010	6	0.005	0.01 (−0.01 to 0.02)	0.35

*Average number of residents per day in homes during period.

the vaccine (Panama in year 1 and Fujian in year 2) differed from the circulating subtype, but antigenic similarities were sufficient for the vaccine to be protective.

Table 1 shows the baseline characteristics of residents in the homes and the median difference between matched pairs (intervention minus control homes). Intervention and control homes had similar baseline characteristics (table 1).

As the interaction between study year and intervention was significant results are reported separately for each year. Table 2 shows the number of outcome events during periods of influenza activity and no activity in intervention and control homes in 2003-4 and 2004-5. The average number of residents in intervention and control homes and event rates per resident period are shown for each period. Table 2 also includes the results of the meta-analysis.

Intervention homes had significantly lower all cause mortality during the influenza period of 2003-4 (rate difference per 100 residents per period −5.0, 95% confidence interval −7.0 to −2.0; P=0.002) compared with control homes (number needed to treat 8.2, 5.8 to 20.4). The effect was not seen during periods of no influenza activity or in the 2004-5 influenza period when influenza levels were low. In the influenza period of 2003-4 significantly lower rates were found for the secondary outcomes in intervention homes compared with control homes: influenza-like illness (rate difference per 100 residents per period −9.0, 95% confidence interval −14.0 to −3.0; P=0.004, number needed to treat 4.5, 2.9 to 13.6), general practitioner consultations for influenza-like illness (−7.0, −12.0 to −2.0; P=0.002, number needed to treat 5.8, 3.4 to 20.4), and admissions to hospital with influenza-like illness (−2.0, −3.0 to 0; P=0.009, number needed to treat 20.4, 13.6 to 102.1). Evidence was found of significant heterogeneity of results for influenza-like illness and associated general practitioner consultations (see bmj.com). No significant differences were found in secondary outcome measures during any other period. The corresponding forest plots are on bmj.com.

Discussion

Vaccinating care home staff against influenza can prevent deaths in residents, morbidity, and associated health service use during periods of moderate influenza activity. The reduction is equivalent to preventing five deaths, two admissions to hospital with influenza-like illness, seven general practitioner consultations for influenza-like illness, and nine cases of influenza-like illness per 100 residents during the period of influenza activity. The numbers of staff vaccinations needed to prevent one death, one case of influenza-like illness, one general practitioner consultation for influenza-like illness, and one admission to hospital with influenza-like illness were 8, 5, 6, and 20. These effects were seen despite high levels of vaccination of residents (poor immune response to vaccine in elderly people can often leave them vulnerable to influenza). In addition to the reductions in mortality and morbidity, the intervention has the potential to substantially reduce health service costs in years with moderate levels of influenza activity, and especially during epidemics.

Lead nurses were not blinded to the intervention, as introducing a placebo arm would have diminished participation rates and would not have been compatible with running a vaccine promotion campaign. We deliberately chose a primary outcome measure (all cause mortality) that is not subject to observer bias, and powered the study accordingly. Nurses in intervention homes might have been less likely to label residents' illnesses as influenza if they strongly believed that the intervention protected residents. This would have led to lower rates of influenza-like illness in intervention homes throughout the study period, not just during the period of influenza activity. Conversely nurses in intervention homes might have been more likely to detect influenza because the vaccination campaign would have raised their awareness.

The intervention was randomly assigned and baseline characteristics of residents in intervention and control homes showed no significant differences that could have accounted for the observed effect. The 4% higher uptake of vaccination in residents in intervention homes could not have accounted for the 25% decrease in mortality or a halving of the influenza-like illness rate. The observed heterogeneity of effect size for influenza-like illness and associated general practitioner consultations is to be expected as the effect depends on introductions of influenza that are stochastic events. Because of heterogeneity we used a random effects model to produce the summary effect estimates.

Influenza activity in 2004-5 was among the lowest recorded since 1988.[23] Nearly twice as much influenza-like illness was reported in 2003-4 as in 2004-5. Because the effect size should be related to the level of circulating influenza we made an a priori decision to analyse the effect separately in the two years. This was supported by a significant interaction between year and intervention on mortality and other outcomes. The direction of effect is the same in both years but the effect is much greater in the first year when influenza activity was substantially higher. The lack of a statistically significant effect in a year with exceptionally low influenza activity is consistent with the hypothesis that the vaccination of staff prevents influenza related morbidity and mortality in residents. Indeed if we had found similar effect sizes in two years with noticeably different levels of influenza activity this would not have been consistent with the hypothesis. The fact that an effect was shown in a year with below average influenza activity suggests that a protective effect would be observed most years. Theoretically the benefits would be substantially greater in epidemic years. The effect might also have been greater if the circulating influenza strain had matched the vaccine strain more closely. Achieving higher vaccine uptake could also have increased effectiveness but is notoriously difficult in healthcare workers. In England's national health service trusts uptake is typically around 15%.[25] Our uptake in full time staff was 48.2% (2003-4) and 43.2% (2004-5) Theoretically better vaccine uptake could have prevented an even greater burden of disease.

A recent systematic review[26] of influenza vaccination of healthcare workers to reduce influenza related outcomes in high risk patients identified only two relevant studies; the first was a pilot for the second.[17 18] The main study showed a reduction in mortality from 22.4% to 13.6% over a six month period, with unusually high influenza activity (Royal College of General Practitioners' influenza-like illness rates peaked at 220 per 100 000). The average vaccine uptake in patients was 48% in intervention wards and 33% in control wards and uptake of vaccine by staff was 51%. After controlling for differences in baseline characteristics the odds ratio for mortality was 0.61 (95% confidence interval 0.36 to 1.04; $P=0.09$). The mortality in our study over the three months in which influenza was circulating in 2003-4 was 15 per 100 residents in control homes and 11 per 100 residents in intervention homes. Our study also showed an important effect on mortality, but this was apparent despite much lower levels of influenza and higher vaccine uptake by residents. No other studies were identified with patient mortality as the primary outcome. One observational study found significantly lower influenza-like illness rates in homes with higher uptake of vaccine by staff even after controlling for vaccine uptake by residents.[27] Another study linked rising rates of hospital staff vaccination to falling rates of nosocomial influenza but could not rule out other causes for the decline.[28]

This study provides strong evidence to support influenza vaccination of care home staff even when vaccine uptake by residents is high. Results are likely to be generalisable to other care homes in the United Kingdom and abroad and may also be applicable to acute hospital settings, in particular elderly care and rehabilitation wards. It has proved difficult to achieve high uptake rates in healthcare workers owing to perceptions that influenza is a relatively trivial illness, concern about side effects, beliefs that the vaccine is ineffective, and lack of time and motivation.[29] Campaigns to promote influenza vaccination among healthcare workers or staff of long term care facilities should emphasise the protection of vulnerable patients and residents as well as the benefits to the individual.

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Competing interests: None declared.

Ethical approval: This study was approved by the London multicentre research ethics committee (No 02/2/56).

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What is already known on this topic

Vaccinating elderly people against influenza reduces sickness and death rates but provides incomplete protection because the immunological response to vaccine is often suboptimal

Two randomised controlled trials of limited size on elderly care wards with low vaccine coverage suggest that vaccinating staff against influenza can reduce death rates during periods of high influenza activity

What this study adds

Vaccinating care home staff against influenza can prevent deaths in residents, morbidity, and associated health service use during periods of moderate influenza activity

The intervention is effective even when there are high levels of vaccination of residents and incomplete vaccine coverage in staff

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Summary

What is already known about this topic?

Skilled nursing facility (SNF) residents, generally older and with more underlying medical conditions than community-dwelling adults, were not included in COVID-19 vaccine clinical trials. Little is known about COVID-19 vaccine effectiveness in SNF residents.

What is added by this report?

A retrospective cohort analysis in two Connecticut SNFs found partial vaccination with Pfizer-BioNTech COVID-19 vaccine (from >14 days after dose 1 through 7 days after dose 2) to be 63% (95% confidence interval = 33%–79%) effective against SARS-CoV-2 infection.

What are the implications for public health practice?

Even with partial vaccination, Pfizer-BioNTech COVID-19 vaccine provides protection to SNF residents. To optimize vaccine impact among this population, high coverage with the complete 2-dose series is recommended.

Figures

Figure 1

Figure 2

Table

References

Related Materials

PDF [198K]

Residents of long-term care facilities (LTCFs), particularly those in skilled nursing facilities (SNFs), have experienced disproportionately high levels of COVID-19–associated morbidity and mortality and were prioritized for early COVID-19 vaccination (*1*,*2*). However, this group was not included in COVID-19 vaccine clinical trials, and limited postauthorization vaccine effectiveness (VE) data are available for this critical population (*3*). It is not known how well COVID-19 vaccines protect SNF residents, who typically are more medically frail, are older, and have more underlying medical conditions than the general population (*1*). In addition, immunogenicity of the Pfizer-BioNTech vaccine was found to be lower in adults aged 65–85 years than in younger adults (*4*). Through the CDC Pharmacy Partnership for Long-Term Care Program, SNF residents and staff members in Connecticut began receiving the Pfizer-BioNTech COVID-19 vaccine on December 18, 2020 (*5*). Administration of the vaccine was conducted during several on-site pharmacy clinics. In late January 2021, the Connecticut Department of Public Health (CT DPH) identified two SNFs experiencing COVID-19 outbreaks among residents and staff members that occurred after each facility's first vaccination clinic. CT DPH, in partnership with CDC, performed electronic chart review in these facilities to obtain information on resident vaccination status and infection with SARS-CoV-2, the virus that causes COVID-19. Partial vaccination, defined as the period from >14 days after the first dose through 7 days after the second dose, had an estimated effectiveness of 63% (95% confidence interval [CI] = 33%–79%) against SARS-CoV-2 infection (regardless of symptoms) among residents within these SNFs. This is similar to estimated effectiveness for a single dose of the Pfizer-BioNTech COVID-19 vaccine in adults across a range of age groups in noncongregate settings (*6*) and suggests that to optimize vaccine impact among this population, high coverage with the complete 2-dose series should be recommended for SNF residents and staff members.

After identification of the first infected SNF resident or staff member through weekly surveillance testing, expanded facility-wide outbreak SARS-CoV-2 testing was performed frequently for residents and staff members at both facilities in accordance with CDC and CT DPH guidelines (*7*). All residents who had not received a positive test result in the preceding 90 days, regardless of symptoms, received a once-weekly (facility A) or twice-weekly (facility B) polymerase chain reaction (PCR) test. Staff members were also tested regularly (once-weekly antigen and once-weekly PCR test at facility A, and once-weekly PCR test at facility B). At both facilities, supplementary antigen testing was performed immediately for any resident or staff member who developed COVID-19 symptoms and for residents who had known COVID-19 exposures.

A retrospective cohort investigation using data from electronic medical record chart abstraction was conducted to assess vaccine effectiveness. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§] The investigation period started on the date of each SNF's first vaccination clinic (December 29, 2020 for facility A and December 21, 2020 for facility B) and ended on February 9, 2021 and February 12, 2021, respectively. Residents were included if they were admitted at either facility during one or more rounds of facility-wide SARS-CoV-2 testing during the week before or any time after their facility's first vaccination clinic. Data on residents were abstracted starting on the date of their SNF's first vaccination clinic or their admission into the facility, whichever occurred later. Electronic medical record data included demographic characteristics, facility admission and discharge dates, vaccination dates, symptoms of COVID-19 occurring within 7 days before or 14 days after a positive test result, presence of underlying medical conditions associated with potential increased risk for severe COVID-19 illness,[¶] and measures of outcome, including hospitalization and death. SARS-CoV-2 test dates, test types, and results were also obtained from the electronic medical record.

A case was defined as any positive PCR- or antigen-based SARS-CoV-2 test result during the investigation period in a resident meeting the cohort inclusion criteria. Case date was defined as either the date of symptom onset or positive SARS-CoV-2 test result, whichever occurred earlier. Positive SARS-CoV-2 test results received before the investigation period were identified for each resident using the Connecticut Electronic Disease Surveillance System.

Person-time began on the date of the facility's first vaccination clinic or the date the resident was admitted, whichever occurred later. Residents stopped contributing person-time to the investigation on the case date, the final facility discharge date or date of death if applicable, or the final day of the investigation period, whichever occurred earlier. Resident person-time was categorized as 1) unvaccinated (days from cohort entry until receipt of first vaccine dose), 2) time before first vaccine dose effect (day 0 [date of vaccination] through day 14 after first dose), 3) partially vaccinated (>day 14 after first dose through day 7 after second dose), or 4) fully vaccinated (>7 days after second dose).

Assuming a common VE against SARS-CoV-2 infection at both facilities, a Cox proportional hazards model with baseline hazard rates stratified by facility was applied to estimate the VE, with VE = 100% × (1−hazard ratio); 95% CIs were calculated using robust CI methods.** Use of a time-to-event analysis was necessary to adjust for expected heterogeneity in risk for infection across the investigation period attributable to underlying outbreak dynamics. Kaplan-Meier curves of SARS-CoV-2 infection were constructed to visualize the cumulative infection-free proportion of residents; 95% CIs were calculated using Greenwood's method.[††] Sensitivity analyses were conducted with exclusion of residents with past confirmed SARS-CoV-2 infection and using two alternative endpoints for partial vaccination (ending on second dose +0 days and second dose +14 days). The time before first dose vaccine effect was excluded from the analysis, because immune status could not be clearly categorized. Small sample sizes precluded separate analyses of VE against symptomatic or severe disease. R statistical software (version 4.0.2; The R Foundation) was used to conduct all analyses.

A total of 463 residents were enrolled, including 142 (31%) from facility A and 321 (69%) from facility B. Demographic characteristics such as age and race were similar in residents at each facility (although ethnicity could not be reported because ethnicity data were missing for 30% of residents); prevalences of underlying conditions that increase the risk for severe COVID-19 illness were also similar in residents at each facility (Table). The median number of high-risk conditions per resident was three; five (1.1%) residents had no underlying high-risk conditions. Among the 463 residents, 115 (24.8%) had confirmed SARS-CoV-2 infection before the investigation period; two of 34 (6%) residents at facility A and 68 of 81 (84%) residents at facility B with past confirmed SARS-CoV-2 infection had a positive test result ≤3 months prior to investigation start.

During the investigation period, 97 cases of SARS-CoV-2 infection occurred, including 40 (41%) at facility A and 57 (59%) at facility B (Figure 1). Including nonspecific symptoms such as malaise, lethargy, and decreased appetite, at least one COVID-19 symptom was reported in 86 (88.7%) cases.[§§] By the date of discharge or the last day of the investigation, 304 residents (65.7%) had received 2 vaccine doses, 72 (15.6%) had received 1 dose only, and 87 (18.8%) had not received any doses. A total of 16,969 person-days were observed during the investigation period, with 39 cases occurring during 3,573 days categorized as unvaccinated person-time, 26 cases during 4,588 days of person-time before first vaccine dose effect, 25 cases during 4,147 days of partially vaccinated person-time, and seven cases during 4,661 days of fully vaccinated person-time.

Estimated effectiveness of partial vaccination in preventing SARS-CoV-2 infection was 63% (95% CI = 33%–79%) and was similar when residents with past SARS-CoV-2 were excluded (VE = 60%, 95% CI = 30%–77%). VE estimates were also similar in both partial vaccination endpoint sensitivity analyses (second dose +0 days VE = 66%, 95% CI = 29%–83%; second dose +14 days VE = 60%, 95% CI = 33%–77%). As a result of the course of the outbreaks at both facilities, most cases occurred toward the start of the investigation period (Figure 2), and because the cohort began at the first vaccination clinic, most of the unvaccinated person-time also occurred toward the start of the investigation period. Thus, once residents became fully vaccinated (second dose +7 days) toward the end of the investigation period, there were insufficient new cases and remaining person-time in the unvaccinated group to serve as a comparator for estimation of full 2-dose VE.

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Discussion

Partial vaccination with the Pfizer-BioNTech COVID-19 vaccine was 63% effective in preventing new SARS-CoV-2 infections in SNF residents, a disproportionately affected population excluded from initial preauthorization vaccine clinical trials. Even during a large disease outbreak in a long-term care setting, the Pfizer-BioNTech vaccine provided protection against SARS-CoV-2 infection, including in older adults aged ≥65 years with a high prevalence of underlying medical conditions. The findings in this report are comparable to other first-dose vaccine efficacy and effectiveness estimates for the Pfizer-BioNTech vaccine for the broader adult population in noncongregate settings. In the phase 3 clinical trial, efficacy during the interval between first and second doses was estimated at 52% (95% CI = 30%–68%) (*8*). In a recent study of the Pfizer-BioNTech vaccine in Israel, effectiveness against PCR-confirmed infection in the general adult population during days 14–20 and 21–27 after the first dose was 46% (95% CI = 40%–51%) and 60% (95% CI = 53%–66%, respectively) (*6*). Effectiveness was somewhat lower during days 14–20 and 21–27 among persons aged ≥70 years (22%; 95% CI = −9%–44% and 50%; 95% CI = 19%–72%, respectively) and among those with three or more underlying medical conditions (37%; 95% CI = 12%–55% and 37%; 95% CI = −1%–62%) (*6*).

In this investigation, nearly 25% of residents had confirmed past SARS-CoV-2 infection. Serologic studies have indicated that preexisting immunity might strengthen the response to a single dose of COVID-19 vaccine (*9*). A sensitivity analysis excluding person-time contributed by residents with confirmed past infections did not substantially alter VE estimates for residents receiving the first vaccine dose. Among residents in this investigation with past confirmed SARS-CoV-2 infection, first-dose vaccination rates were >90%, and only one reinfection was documented, limiting the ability to determine the impact of past infection.

The findings in this report are subject to at least seven limitations. First, because there were no clear factors that would differentially affect the risk for infection among residents within either facility, such as units with higher attack rates or different infection prevention practices, each observation in the model was treated as independent. If risk was not independent, this could have biased the VE estimates. Second, 2-dose VE estimates were not possible because unvaccinated cases and person-time after second-dose vaccination clinics were insufficient. Third, small sample sizes did not allow for analyses of secondary endpoints, such as effectiveness against symptomatic illness, hospitalization, or death. Fourth, although there was no change in guidance around outbreak control measures such as cohorting and other infection prevention and control strategies concurrent with vaccine introduction, had these measures been implemented differently for vaccinated and unvaccinated residents, VE estimates could have been biased. Fifth, racial minority groups were underrepresented in this investigation compared with the general population of older adults, and ethnicity data were missing for approximately one third of residents, which might affect generalizability to other SNF populations. Sixth, although excluding person-time from residents with known past confirmed SARS-CoV-2 infection did not influence VE estimates in this analysis, there could have been residents with unknown past infection who could still have acted as a source of potential bias. Finally, unrecognized underlying differences between vaccinated and unvaccinated residents might have confounded the effectiveness estimates. Strengths of the investigation include accurate collection of vaccination data through direct abstraction from resident electronic medical records and active ascertainment of SARS-CoV-2 infection through frequent, facility-wide resident testing.

Findings from this retrospective cohort analysis demonstrate that partial vaccination with the Pfizer-BioNTech COVID-19 vaccine was associated with a significant reduction in the risk for SARS-CoV-2 infection among SNF residents. These results, coupled with the findings from a previous study among comparable older adult populations in Israel that reported more robust protection after the second dose (*6*), suggest that complete 2-dose vaccination is an important strategy for preventing COVID-19 in this disproportionately affected population. Further study of this population should continue as larger sample sizes become available. LTCFs and jurisdictions should actively ensure that they have plans in place for continued allocation and administration of COVID-19 vaccines to residents and staff members (*10*).

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§ This investigation was defined as having met the requirements for public health surveillance as outlined in 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

¶ Conditions based on CDC guidelines identifying conditions associated or potentially associated with risk for severe COVID-19 illness. List of conditions available at https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

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§§ Clinician judgement during chart abstraction was used to distinguish COVID-19 symptoms from those potentially associated with vaccination or other illness. Symptoms had to be new onset within 7 days before or 14 days after a positive test result. Symptom-onset date was available for 80 of 86 cases classified as symptomatic (93%). Among those 80 cases for which symptom-onset date was available, only four (5%) had a symptom-onset date within the 48 hours after receiving a vaccine.

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TABLE. Demographic characteristics, COVID-19 vaccination status, and SARS-CoV-2 infection, symptom, and outcome information among residents of two skilled nursing facilities — Connecticut, December 21, 2020–February 12, 2021

Return

	No. (%) of residents*			
	Total	Facility A	Facility B	
Characteristic	(N = 463)	(n = 142)	(n = 321)	p-value†,§
Sex				
Female	**294 (63.5)**	82 (57.8)	212 (66.0)	0.09
Male	**169 (36.5)**	60 (42.3)	109 (34.0)	
Age group, yrs				
<60	**23 (5.0)**	18 (12.7)	5 (1.6)	<0.001
60–64	**19 (4.1)**	12 (8.5)	7 (2.2)	
65–69	**34 (7.3)**	16 (11.3)	18 (5.6)	
70–74	**46 (9.9)**	14 (9.9)	32 (10.0)	
75–79	**56 (12.1)**	17 (12.0)	39 (12.2)	
80–84	**54 (11.7)**	15 (10.6)	39 (12.2)	
≥85	**231 (49.9)**	50 (35.2)	181 (56.4)	
Race¶				
American Indian/Alaska Native	**1 (0.2)**	0 (0.0)	1 (0.3)	0.57§
Asian	**5 (1.1)**	1 (0.7)	4 (1.3)	
Black	**16 (3.5)**	5 (3.5)	11 (3.4)	
Native Hawaiian/Pacific Islander	**1 (0.2)**	0 (0.0)	1 (0.3)	
White	**428 (92.4)**	135 (95.1)	293 (91.3)	
Unknown	**12 (2.6)**	1 (0.7)	11 (3.4)	
High-risk medical conditions**				

Characteristic	No. (%) of residents* Total (N = 463)	Facility A (n = 142)	Facility B (n = 321)	p-value†,§
Obesity	**44 (9.5)**	16 (11.3)	28 (8.7)	0.39
Chronic kidney disease	**92 (19.9)**	32 (22.5)	60 (18.7)	0.34
End-stage renal disease requiring dialysis	**3 (0.7)**	2 (1.4)	1 (0.3)	0.22§
Diabetes mellitus (type I or II)	**131 (28.3)**	51 (35.9)	80 (24.9)	0.02
Cancer (not in remission)	**28 (6.1)**	9 (6.3)	19 (5.9)	0.86
Autoimmune disease	**33 (7.1)**	13 (9.2)	20 (6.2)	0.26
Chronic heart or cardiovascular disease	**186 (40.2)**	55 (38.7)	131 (40.8)	0.67
Hypertension	**352 (76.0)**	103 (72.5)	249 (77.6)	0.24
COPD/Sleep apnea/Other chronic respiratory condition	**94 (20.3)**	34 (23.9)	60 (18.7)	0.20
Immunocompromising conditions††	**9 (1.9)**	4 (2.8)	5 (1.6)	0.47§
Neurologic/Neurodevelopmental disorders§§	**346 (74.7)**	105 (73.9)	241 (75.1)	0.80
Other chronic diseases	**66 (14.3)**	7 (4.9)	59 (18.4)	0.001
None of these conditions	**5 (1.1)**	1 (0.7)	4 (1.2)	0.10§
History of past COVID-19				
Yes	**115 (24.8)**	34 (23.9)	81 (25.2)	0.76
>3 months before investigation start	**45 (9.7)**	32 (22.5)	13 (4.0)	<0.001
≤3 months before investigation start	**70 (15.1)**	2 (1.4)	68 (21.2)	
Vaccination coverage among all residents¶¶				
None	**87 (18.8)**	32 (22.5)	55 (17.1)	0.09
1 dose only	**72 (15.6)**	27 (19.0)	45 (14.0)	
2 doses	**304 (65.7)**	83 (58.5)	221 (68.8)	
Interval between vaccine doses				
Days between doses 1 and 2, median (range)	**21 (21–42)**	21 (21–42)	21 (21–32)	N/A
Cases				
All cases	**97 (21.0)**	40 (28.2)	57 (17.8)	0.01
Symptomatic, no. (% of cases)	**86 (88.7)**	33 (82.5)	53 (93.0)	0.19§

Characteristic	No. (%) of residents* Total (N = 463)	Facility A (n = 142)	Facility B (n = 321)	p-value†,§
Reported symptoms, no. (% of cases)				
None	**11 (11.3)**	7 (17.5)	4 (7.0)	0.19§
Fever and chills	**24 (24.7)**	5 (12.5)	19 (33.3)	0.02
Cough	**63 (65.0)**	21 (52.5)	42 (73.7)	0.03
Shortness of breath/Difficulty breathing	**18 (18.6)**	8 (20.0)	10 (17.5)	0.76
Myalgias	**7 (7.2)**	0 (0.0)	7 (12.3)	0.04§
Headaches	**3 (3.1)**	2 (5.0)	1 (1.8)	0.57§
Sore throat	**5 (5.2)**	0 (0.0)	5 (8.8)	0.08§
New loss of taste or smell	**1 (1.0)**	0 (0.0)	1 (1.8)	N/A
Congestion/Rhinorrhea	**16 (16.5)**	6 (15.0)	10 (17.5)	0.74
Abdominal pain	**3 (3.1)**	2 (5.0)	1 (1.8)	0.57§
Nausea/Vomiting	**12 (12.4)**	2 (5.0)	10 (17.5)	0.11§
Diarrhea	**6 (6.2)**	1 (2.5)	5 (8.8)	0.40§
Confusion/Altered mental status	**21 (21.7)**	11 (27.5)	10 (17.5)	0.24
Other***	**65 (67.0)**	26 (65.0)	39 (68.4)	0.72
Vaccination status on case date, no. (% of cases)				
Unvaccinated	**39 (40.2)**	15 (37.5)	24 (42.1)	0.16§
Before dose 1 effect (day 0 through day 14 after dose 1)	**26 (26.8)**	15 (37.5)	11 (19.3)	
Partially vaccinated (>day 14 after dose 1 through day 7 after dose 2)	**25 (25.8)**	9 (22.5)	16 (28.1)	
Fully vaccinated (>7 days after dose 2)	**7 (7.2)**	1 (2.5)	6 (10.5)	
Outcomes,††† no. (% of cases)				
Hospitalization	**15 (15.5)**	4 (10.0)	11 (19.3)	0.21
Vital status dead or unknown				
Death from COVID-19	**17 (17.5)**	7 (17.5)	10 (17.5)	0.55§
Death after diagnosis (no cause specified)	**4 (4.1)**	1 (2.5)	3 (5.3)	
Vital status unknown	**3 (3.1)**	0 (0.0)	3 (5.3)	

Abbreviations: COPD = chronic obstructive pulmonary disease; N/A = not applicable.

* Percentages might not sum to 100% because of rounding.

† P-values for the comparisons between facilities apply Pearson's chi-square test for independence unless marked. For mutually exclusive categories of a characteristic a single p-value is reported. For characteristics for which more than one category might be true for a resident (e.g., symptoms), individual p-values are reported for each category.

§ In cases with cell counts <5, Fisher's exact test was used to calculate the p-value.

¶ Ethnicity is not reported because data were missing for 30% of residents.

** Conditions associated with potential increased risk for severe COVID-19 illness per CDC guidelines.

†† HIV coinfection (not virally suppressed), chemotherapy within past 12 months, solid-organ or bone marrow transplant, long-term steroid use (20 mg per day for >1 month), taking immunosuppressants, or taking tumor necrosis factor-alpha inhibitors.

§§ Examples include seizure disorders such as epilepsy, Alzheimer disease, dementia, traumatic brain injuries, and stroke.

¶¶ Vaccination is reported as the percentage of all residents included in the investigation that received no dose, 1 dose, or 2 doses of Pfizer-BioNTech COVID-19 vaccine by the date of their discharge from the facility or the end of the investigation if they were still admitted to the facility. Absolute coverage in the facility changed daily because of changes in census.

*** Other symptoms included lethargy, fatigue, generalized weakness, malaise, decreased appetite or loss of appetite, and agitation.

††† Case outcomes include minimum number of confirmed COVID-19–related hospitalizations and COVID-19 deaths confirmed by the Office of the Chief Medical Examiner. Hospitalizations and deaths that occurred after the investigation period were not ascertained.

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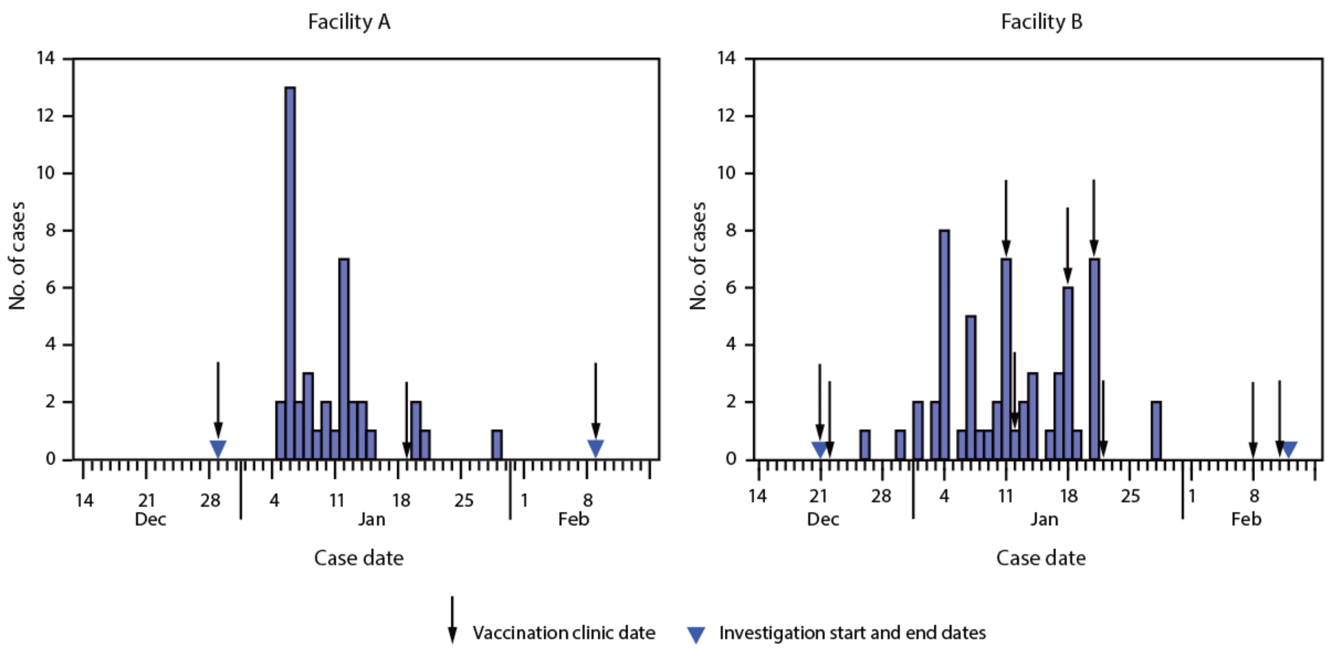
FIGURE 1. New SARS-CoV-2 cases* among residents of two skilled nursing facilities, by case date† — Connecticut, December 21, 2020–February 12, 2021§



* Any positive SARS-CoV-2 polymerase chain reaction or antigen test result.

† Symptom onset date or positive test result date, whichever occurred earlier.

§ Investigation period was December 29, 2020–February 9, 2021 for facility A and December 21, 2020–February 12, 2021 for facility B.

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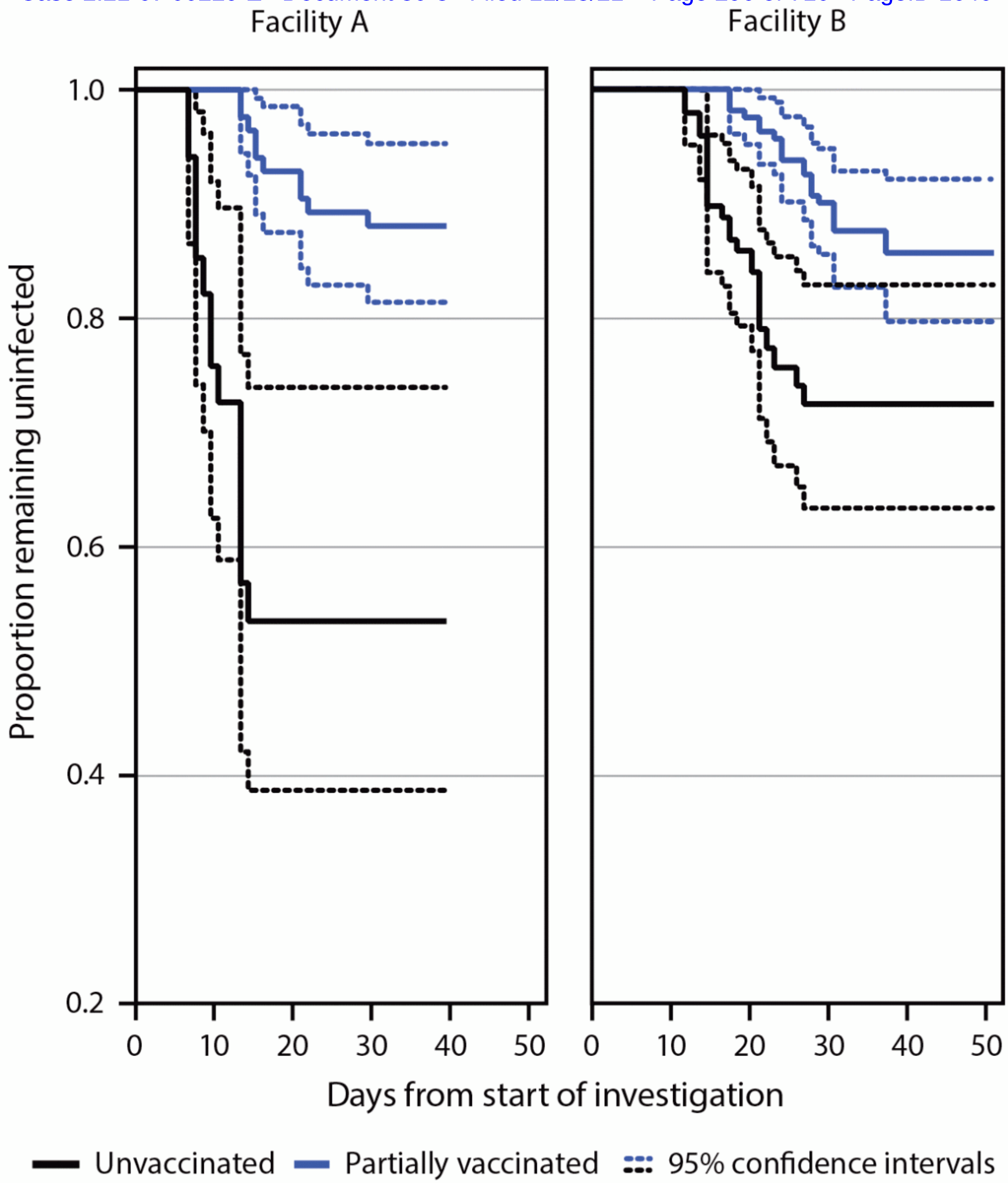
FIGURE 2. Proportion of skilled nursing facility residents who remained uninfected with SARS-CoV-2 during the investigation period,* by COVID-19 vaccination status† and facility — Connecticut, December 21, 2020–February 12, 2021



* Investigation period was December 29, 2020–February 9, 2021 for facility A and December 21, 2020–February 12, 2021 for facility B.

[†] Vaccination status is classified as unvaccinated or partially vaccinated. Partially vaccinated refers to the time from day 14 after first dose of Pfizer-BioNTech COVID-19 vaccine through day 7 after the second dose. Greenwood's method was used to estimate confidence intervals around the Kaplan-Meier estimator.

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Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial

William F Carman, Alexander G Elder, Lesley A Wallace, Karen McAulay, Andrew Walker, Gordon D Murray, David J Stott

Summary

Background Vaccination of health-care workers has been claimed to prevent nosocomial influenza infection of elderly patients in long-term care. Data are, however, limited on this strategy. We aimed to find out whether vaccination of health-care workers lowers mortality and the frequency of virologically proven influenza in such patients.

Methods In a parallel-group study, health-care workers in 20 long-term elderly-care hospitals (range 44–105 patients) were randomly offered or not offered influenza vaccine (cluster randomisation, stratified for policy for vaccination of patients and hospital size). All deaths among patients were recorded over 6 months in the winter of 1996–97. We selected a random sample of 50% of patients for virological surveillance for influenza, with combined nasal and throat swabs taken every 2 weeks during the epidemic period. Swabs were tested by tissue culture and PCR for influenza viruses A and B.

Findings Influenza vaccine uptake in health-care workers was 50·9% in hospitals in which they were routinely offered vaccine, compared with 4·9% in those in which they were not. The uncorrected rate of mortality in patients was 102 (13·6%) of 749 in vaccine hospitals compared with 154 (22·4%) of 688 in no-vaccine hospitals (odds ratio 0·58 [95% CI 0·40–0·84], p=0·014). The two groups did not differ for proportions of patients positive for influenza infection (5·4% and 6·7%, respectively); at necropsy, PCR was positive in none of 17 patients from vaccine hospitals and six (20%) of 30 from no-vaccine hospitals (p=0·055).

Interpretation Vaccination of health-care workers was associated with a substantial decrease in mortality among patients. However, virological surveillance showed no associated decrease in non-fatal influenza infection in patients.

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See Commentary page ???

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Introduction

Influenza is one of the leading causes of respiratory infection.[1] It remains an important cause of death in elderly people, with most excess mortality in patients older than 65 years.[2] Environmental factors play an important part in determining the risk of infection, and grouping of frail elderly people in long-term care creates an environment that is likely to allow rapid spread of influenza infection. Case-control studies have shown that influenza vaccination of elderly people in long-term care is associated with decreased risk of pneumonia and death.[3] This strategy is supported by The Chief Medical Officers in the UK and by the Centers for Disease Control in the USA, who recommend influenza vaccination for elderly people who have chronic disease or who are in long-term care.[4,5] However, the protection afforded by vaccination of frail elderly patients is frequently incomplete, probably because of impaired immune function through inability to develop adequate protective circulating antibody concentrations after vaccination.[6,7]

Vaccination of health-care workers has been suggested as an additional or alternative strategy to lower rates of nosocomial transmission to patients at high risk of complications. We have found serological evidence of influenza infection in 23% of hospital staff in a winter season.[8] The potential is therefore high for influenza to be brought into elderly-care homes by susceptible health-care workers, and for infection to be transmitted to other health-care workers and to patients. In a previous pilot study, we found that vaccination of health-care workers was associated with a decrease in mortality of elderly patients in long-term care from 17% to 10% over a winter season.[9]

We did a multicentre, randomised, controlled study to find out whether vaccination of health-care workers can lower mortality and the frequency of laboratory-proven influenza infection in elderly patients in long-term-care hospitals.

Methods

Study design

The study was a parallel-group design with cluster randomisation. Clusters were based on 20 UK National Health Service medical long-term-care geriatric hospitals across west and central Scotland. Hospitals were randomly allocated to be offered routine vaccination of health-care workers or not to be offered vaccination. Randomisation of clusters was balanced and stratified for policy for vaccination of patients and size of hospital. Hospitals were paired according to number of beds and policy for vaccination of patients, and one was chosen from each pair by random-numbers table for health-care workers to be vaccinated. Ten hospitals had a policy of vaccinating all consenting patients without contraindications, and in the other ten, the policy was to vaccinate primarily on request from patients or their relatives. Randomisation of sites was done by the study statistician (independent of the clinicians involved in the study). The study was approved by all the relevant local-

hospital ethics committees. We obtained written informed consent from health-care workers who agreed to be vaccinated. Witnessed verbal consent was obtained from patients for nose and throat swabs to be taken.

In hospitals offered vaccination, the day and night nurses, doctors, therapists, porters, and ancillary staff (including domestic staff and ward cleaners) were given a letter informing them of the study and asking whether they would be willing to be interviewed and considered for influenza vaccination. Structured interviews to find any contraindications to vaccination and administration of vaccine to suitable health-care workers were done at the places of work by a team of trained study nurses. The vaccination programme was completed by the end of October, 1996.

All patients who were resident in the hospitals on Oct 31, 1996, were entered into the study. We recorded patients' ages and sex and measured degree of disability with the modified (20-point) Barthel index.[10] Patients admitted after the census date were recorded but excluded from the study. We recorded mortality among patients during 6 months, from Nov 18, 1996, to March 31, 1997.

At the end of the surveillance period (March 31, 1997) we sent questionnaires to the largest subgroup of health-care workers, the ward nursing staff (trained and untrained) to complete anonymously, asking whether they had received influenza vaccine during the autumn or winter. The response enabled us to estimate the uptake of influenza vaccine in health-care workers in hospitals not offered routine vaccination.

Virological surveillance and laboratory analyses

We selected a random sample of 50% of patients in each hospital for prospective virological monitoring. Randomisation was done centrally by computer-generated random numbers. Routine weekly community monitoring reports of influenza produced by the Scottish Centre for Infection and Epidemiological Health from returns from family-physician practices were used to define the start of the winter epidemic, at which time we started virological surveillance.

Combined nose and throat swabs on single swabs were taken by trained nurses every 2 weeks from Dec 14, 1996, until Feb 14, 1997, which gave a maximum of four samples per patient over this period. Swabs were placed into 1·8 mL viral transport medium (Life Technologies, Paisley, UK) and delivered in ice to the Institute of Virology on the day of collection or kept overnight in the fridge and transported on ice the next day. A sample was removed on receipt and stored at −70°C for reverse-transcriptase PCR (RT-PCR) analysis. At the times when study nurses took routine samples, they took additional opportunistic nose and throat swabs from non-randomised patients who the ward nurses thought had an influenza-like illness. The ward nursing staff were asked to take routine nasal swabs within 12 h of death for any patient who died.

Tissue cultures for isolating the Madin Darby canine kidney (MDCK), and Rhesus monkey kidney (RMK) cells (BioWhittaker, Verviers, Belgium) were seeded into 96-well plates between 24 h and 48 h before sample inoculation. Samples (25 μL) were inocculated in duplicate on to monolayers and maintained in serum-free medium at 34°C for 7 days, with trypsin (0·25 ng/mL) added to the MDCK cell line only. After 7 days, the cells were fixed in the 96-well plates with a 1:1 acetone and methanol mixture (each 50% volume) and air dried. Direct immunofluorescence of influenza A and B virus in these cells was done with 1:2 dilutions of fluorescein conjugated monoclonal antibodies (Imagen Influenza A and B, DAKO Diagnostics Ltd, Cambridge, UK).

To extract nucleic acid and synthesise cDNA, 100 μL samples from the patients randomised to routine virological surveillance were pooled (two individuals' samples from different time points in one pooled sample). RNA was extracted with the High Pure Viral RNA kit (Roche Diagnostic, Penzberg, Germany). Viral RNA was eluted in 50 μL water, and cDNA synthesis was done with random primers

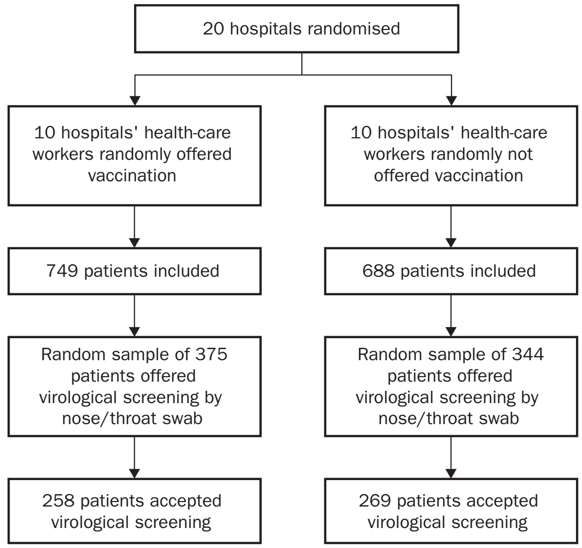

Figure 1: **Trial profile**

Detection of influenza A (H3 and H1) and B viruses by multiplex RT-PCR was done with nested primer sets from the matrix gene regions.[11] under optimum conditions.[12] A nested PCR was done with TaqStart antibody (Clontech, Palo Alto, USA) in a "hot-start" PCR reaction.

Statistical analysis

Power calculations for mortality among patients were based on our previous study of 1994–95. We calculated that, with a total sample size of 1600 patients in 20 hospitals, we would have at least 80% power to detect a decrease in mortality from 15% to 10% at 5% significance (two-tailed), with allowance for the clustered design.[13] Power calculations for virological sampling showed that 500 patients would be required to give 80% power at 5% significance (two-tailed) to detect a decease in influenza infection rates from 25% to 15%.

We decided a priori to do analysis by calculation of simple summary statistics for each cluster and then do analysis of these summary values. This approach lacks sensitivity but is robust, transparent, and valid.[14] We compared mortality rates in the two groups with the Mann-Whitney test. After the end of the study, it became apparent that hospitals were not well matched for patients' Barthel Scores and patients' influenza-vaccination rates. We therefore considered the effect of adjusting the primary analysis for these imbalances. Incomplete data for patient-level covariates meant that a full multilevel approach to the analysis was not possible without making strong, implausible, and untestable assumptions about the mechanisms that led to the incomplete data. Instead, we calculated summary statistics to describe the mix of patients in each hospital, and these values were included in a multiple linear-regression analysis. The response variable in these analyses was the empirical logit of each hospital's mortality rate that is, the natural logarithm of the odds on death. A standard continuity correction was made by addition of 0·5 to the number of deaths and the number of survivors when the odds were calculated. The logit transformation was used to satisfy the distributional assumptions required for the regression analysis and to allow

	Vaccine group	No-vaccine group
Number of hospitals	10	10
Total number (range) of patients	749 (44–109)	688 (44–105)
Mean (SD) age (years)	82·0 (8·8)	82·5 (8·6)
Proportion (range) men	29% (14–45)	31% (18–50)
Median (range) Barthel score	5 (3–7·5)	3 (1–5)
Mean proportion (range) influenza-vaccine uptake	48 (0–94)	33 (0–70)

Table 1: **Baseline characteristics of patients**

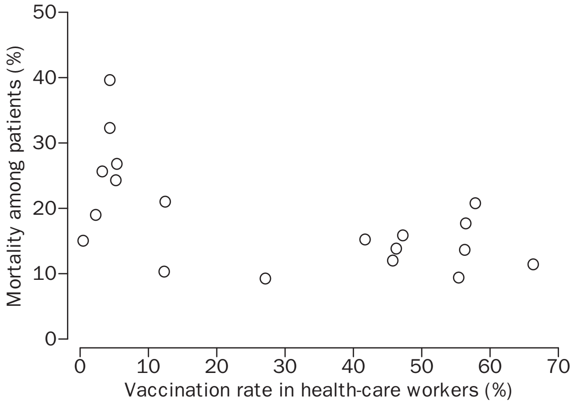

Figure 2: **Vaccination uptake in health-care workers and mortality among patients for each hospital**

the effect of the vaccination to be expressed as an odds ratio. Results were significant at p<0·05.

Results

1217 health-care workers were employed in the hospitals offered influenza vaccine; 620 (50·9%) were vaccinated (figure 1). The questionnaires from the same sites showed an uptake of 49·8% in respondents (trained and untrained nurses), compared with 4·8% in hospitals not offered vaccine. The questionnaire return rates were estimated to be 68% from nurses in vaccine hospitals and 49% in no-vaccine hospitals.

1437 patients (749 in vaccine hospitals 688 in no-vaccine hospitals) were included in the study (figure 1). The groups were well matched for age and sex (table 1). The uncorrected mortality among patients was 102 (13·6%) of 749 in vaccine hospitals compared with 154 (22·4%) of 688 in no-vaccine hospitals (odds ratio 0·58 [95% CI 0·40–0·84], p=0·014]). The relation between vaccination uptake in health-care workers and mortality among patients and between vaccination uptake in patients and mortality are shown in figures 2 and 3, respectively. Regression analyses showed significant associations between mortality among patients and rate of vaccination of patients per site, median Barthel score per site, mean age per site, and proportion of male patients per site. The adjusted odds ratios for the effects of vaccination of health-care workers on mortality among patients are shown in table 2.

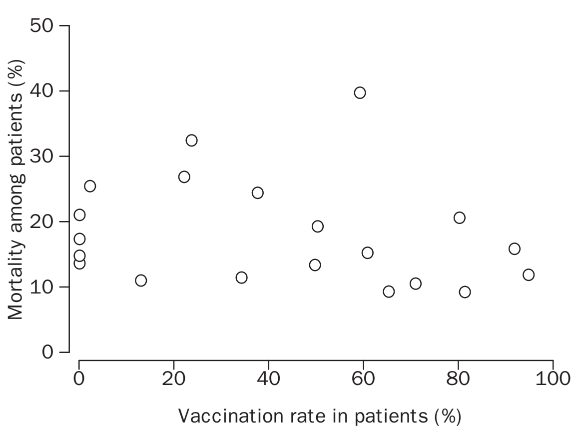

Figure 3: **Vaccination uptake and mortality among patients for each hospital**

Statistical model	Odds ratio (95% CI)	p
Unadjusted analysis	0·58 (0·40–0·84)	0·011
Adjusted for Barthel score	0·62 (0·41–0·95)	0·044
Adjusted for vaccination of patients	0·60 (0·39–0·90)	0·026
Adjusted for Barthel score, age, and sex	0·59 (0·37–0·95)	0·044
Adjusted for Barthel, age, sex, and vaccination of patients	0·61 (0·36–1·04)	0·092

Table 2: **Odds ratios for the impact of health-care-worker vaccination on mortality in patients**

	Vaccine hospitals	No vaccine hospitals
Routine surveillance		
Total patients	258	269
Culture positive		
Influenza A	3 (1%)	9 (3%)
Influenza B	3 (1%)	1 (0·4%)
PCR positive		
Influenza A	10 (4%)	17 (6%)
Influenza B	4 (2%)	1 (0·4%)
Patients with symptoms		
Total patients	29	39
Culture positive		
Influenza A	0	1 (3%)
Influenza B	0	0
PCR positive		
Influenza A	3 (10%)	5 (13%)
Influenza B	0	1 (3%)
Samples taken at death		
Total patients	17	30
Culture positive		
Influenza A	0	4 (13%)
Influenza B	0	0
PCR positive		
Influenza A	0	6 (20%)
Influenza B	0	0

Table 3: **Results of tissue culture and PCR for influenza infection on nose and throat swabs**

A subgroup of 719 patients (375 in vaccine hospitals and 344 in no-vaccine hospitals) underwent routine virological surveillance. Combined nose and throat swabs were obtained from 527 (73%) of these patients (258 in vaccine hospitals, 269 in no-vaccine hospitals). At least three samples were obtained in each of 225 (60%) patients in hospitals offered vaccine, and 219 (64%) in hospitals not offered vaccines. In total, 1798 samples were collected from the 527 patients (mean 3·4 samples per patient). 68 additional opportunistic swabs were taken from patients who were not part of the screening programme but who had symptoms consistent with influenza or upper-respiratory-tract infection (29 in vaccine hospitals, 39 in no-vaccine hospitals). 47 samples were taken from patients after death (17 in vaccine hospitals, 30 in no-vaccine hospitals). 21 samples were positive by tissue culture, compared with 47 by PCR (table 3). All samples that were positive by tissue culture were also positive by PCR. In the samples taken at death, none of 17 was positive from patients in hospitals offered vaccine, compared with six (20%) of 30 from those in hospitals offered no vaccine (p=0·055). The two groups did not differ significantly in the proportions of swabs positive in culture or PCR for routine (p=0·42) or opportunistic samples (p=0·54), although there was a higher rate of influenza infection in hospitals offered no vaccine (table 3). No patient had more than one epidose of influenza during the study and no patient had a dual infection (influenza A plus B).

Eight of 11 influenza-A-positive samples were found in the second of the routine virological surveillance samples, which were taken in the first 2 weeks in January at the peak of the community influenza A epidemic.[15] A

similar pattern was seen for PCR samples taken at death (five of six positive).

Discussion

We achieved a vaccine uptake in health-care workers of about 50%. This proportion is slightly lower than the 60% vaccinated in our previous study,[9] but is similar to other vaccination programmes of health-care workers in long-term-care homes in the USA that gave compliance rates of 46–54%.[16] Our programme of influenza vaccination was associated with a decrease in mortality among patients. The effects of various possible confounders must, however, be taken into account before this association can be accepted as causal.

Patients from hospitals in which health-care workers were routinely offered vaccine had slightly lower Barthel scores and were more likely to receive influenza vaccine than patients from the no-vaccine hospitals. Disability is a strong predictor of fatal outcome of infections in elderly nursing-home residents.[17] However the between-group difference in baseline Barthel score, although significant, was small and, therefore, unlikely to have been an important contributor to the differences in mortality between the two groups of patients, which is supported by the multivariate regression analysis.

The differences in vaccination uptake in patients were unexpected, since in the study design we had stratified randomisation of hospitals according to their policies for vaccination of patients. Our programme of vaccination of health-care workers may have raised awareness of the risks of influenza for elderly patients and led to an increased use of influenza vaccine in hospitals offered vaccination compared with previous practice. The higher uptake of influenza vaccine in patients in those hospitals than in hospitals not offered vaccination (48 *vs* 33%) could be a contributory factor to lower mortality among patients. The impact of vaccination of health-care workers on mortality among patients was, however, stable in various statistical models, which suggests that the unadjusted estimate of the odds ratio is not biased because of confounding. As expected, the precision of the estimate declines in more complex models that used many variables, based on only 20 observations. The mortality results are similar to a previous smaller-scale study that we did in the winter of 1994–95, in which we found that vaccination of health-care workers was associated with a decrease in mortality from 17% to 10% in elderly long-term-care patients.[9] That study was done in 12 sites and involved 1059 patients. There is good evidence, therefore, that a programme of influenza vaccination of health-care workers substantially lowers mortality among elderly patients in long-term care, probably through prevention of nosocomial transmission.

We made a deliberate decision not to use a blinded study design with placebo vaccination of health-care workers. We wanted to investigate effects of a programme offering vaccination to health-care workers compared with the current UK practice of not routinely offering vaccine. The primary endpoint, mortality, was objective and not subject to observer bias. We were concerned that the use of masking and placebo vaccine would lower the participation rate of health-care workers, and would potentially undermine the whole study.

The observed lack of any clear association of vaccination uptake in patients with lowered mortality is noteworthy. The elderly patients we studied were more disabled than those in UK private nursing homes or government-funded residential homes.[18] Many UK geriatricians believe that routine influenza vaccination of this frail group of long-term-care patients is unlikely to be beneficial,[19] which is reflected in the variable use of influenza vaccine under normal policy. Previous case-control studies of elderly people in residential care that have shown benefits through decreases in the number of cases of pneumonia and of deaths have generally looked at fitter elderly people than we studied.[3] Although we did not design our study primarily to find out whether vaccination of patients lowers mortality, we found no association between vaccination uptake rates in patients and mortality. The results are also similar to our previous study.[9] The degree of protection offered by vaccination is significantly decreased in frail and disabled elderly people.[7,20] Our data also suggest that vaccination of this subgroup of elderly people does not influence mortality.

Despite an advanced programme of virological surveillance, including tissue culture and PCR, we saw no significant difference in laboratory-proven influenza infection in randomly sampled patients from hospitals offered vaccine compared with those not offered vaccine, although more influenza was detected (by culture and PCR) in samples from patients in no-vaccine hospitals. The positive detection rate in these hospitals of 6·7% was much lower than the anticipated rate of 25% used in our power calculations. Fortnightly nose and throat swabs may have missed some influenza infections that occurred and resolved between sampling dates. Furthermore many patients declined to provide all four planned samples. Although the sampling period was targeted at the peak time for influenza, some patients may have become infected outside this surveillance period. Our detection rate for influenza is probably, therefore, an underestimate of the true infection rate. Samples taken at death were positive in 20% of deaths in the no-vaccine hospitals compared with none in the vaccine hospitals, consistent with a major effect of vaccination of health-care workers on fatal influenza in frail elderly patients. Samples were obtained, however, from only a small proportion of all deaths, and so these results should be interpreted cautiously.

PCR was more than twice as sensitive as tissue culture to detect influenza. This difference occurred in some samples because detection of influenza was improved when sampling was done during periods of low viral load in the upper respiratory tract, and in others because viability of the virus may have been lost during transport and processing of samples. PCR contamination seemed not to have been an issue since no patients had more than one positive sample or had a dual infection (influenza A and B). All positive results on culture were also detected by PCR. Our results further confirm that PCR is probably better than tissue culture for laboratory confirmation of influenza, and should be used as the primary assay in clinical studies in which laboratory confirmation is required.[21]

The Wuhan H3N2 variant appeared for the last time in the year of the study, 1996–97. There was a good match in the study year between the prevailing influenza variants and those in the vaccine (H3N2 and H1N1 and

B variants). A good match between the vaccine and prevailing influenza virus is likely to be important in obtaining the maximum protective effect of vaccination.

Contributors

All investigators contributed to the design, writing, and redrafting of the paper. William Carman supervised the virological laboratory analyses. Alexander Elder contributed to the supervision and training of the study nurses, Lesley Wallace and Karen McAuley did the laboratory analyses. Gordon Murray prepared the randomisation scheme and analysed the main mortality data. David Stott supervised the running of the clinical part of the study, and took the lead role in writing and redrafting the paper.

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Emergency Use Authorization

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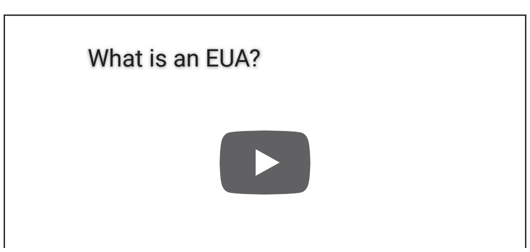
About Emergency Use Authorizations (EUAs)

The Emergency Use Authorization (EUA) authority allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats including infectious diseases, by facilitating the availability and use of medical countermeasures (/emergency-preparedness-and-response/about-mcmi/what-are-medical-countermeasures) (MCMs) needed during public health emergencies.



Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act (/federal-food-drug-and-cosmetic-act-fdc-act)), when the Secretary of HHS declares that an emergency use authorization is appropriate, FDA may authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when certain criteria are met, including there are no adequate, approved, and available alternatives. The HHS declaration to support such use must be based on one of four types of determinations of threats or potential threats by the Secretary of HHS, Homeland Security, or Defense.

Please note: a determination under section 319 of the Public Health Service Act that a public health emergency exists, such as the one issued on January 31, 2020 (https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx), does not enable FDA to issue EUAs. On February 4, 2020, the HHS Secretary determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Subsequent HHS declarations supporting use of EUAs and based on this determination are described in the blue boxes below.

Information on terminated and revoked EUAs can be found in archived information (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information).

Public Readiness and Emergency Preparedness Act (PREP Act)

Information on the PREP Act can be found here (https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx).

The PREP Act amended the Public Health Service Act (PHS Act) to add section 319F-3 (42 U.S.C. 247d-6d). The HHS Secretary has issued several Declarations pursuant to section 319F-3 of the PHS Act to provide liability immunity for activities related to medical countermeasures against COVID-19.

PREP Act - COVID-19 Related Information

- Notice of Declaration under the Public Readiness and Emergency Preparedness Act for medical countermeasures against COVID-19 (https://www.federalregister.gov/documents/2020/03/17/2020-05484/declaration-under-the-public-readiness-and-emergency-preparedness-act-for-medical-countermeasures) (February 4, 2020)
- COVID-19 PREP Act Declarations and Amendments (HHS) (https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx#covid)
- Advisory Opinion 02-02 on the PREP Act and the Secretary's Declaration under the Act (https://www.hhs.gov/sites/default/files/advisory-opinion-20-02-hhs-ogc-prep-act.pdf) (PDF, 278 KB, May 19, 2020)

Guidance

In January 2017, FDA finalized the guidance: Emergency Use Authorization of Medical Products and Related Authorities (/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities). For more information, please see the January 13, 2017 Federal Register notice (https://www.federalregister.gov/documents/2017/01/13/2017-00721/emergency-use-authorization-of-medical-products-and-related-authorities-guidance-for-industry-and).

Printable PDF (288 KB) (/media/97321/download)

In addition, in January 2014, FDA issued a question and answer document (/media/87718/download) (PDF, 792K) to respond to questions raised by public health stakeholders about PAHPRA's amendments to the EUA authority and establishment of new authorities related to the emergency use of MCMs during CBRN emergencies.

Coronavirus Disease 2019 (COVID-19) EUA Information

- **Coronavirus Disease (COVID-19) updates from FDA** (/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19)
- **Detailed Information for all COVID-19 EUAs, including authorizations and fact sheets**
  - Vaccines
  - Drug and Biological Therapeutic Products
  - COVID-19 EUAs for Medical Devices (/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices), including:
    - Blood Purification Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/blood-purification-devices-euas)
    - Continuous Renal Replacement Therapy and Hemodialysis Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/continuous-renal-replacement-therapy-and-hemodialysis-devices-euas)
    - In Vitro Diagnostics EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas)
    - Decontamination Systems for Personal Protective Equipment EUAs (/about-fda/page-not-found)
    - Infusion Pump EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/infusion-pump-euas)
    - Personal Protective Equipment EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/personal-protective-equipment-euas)
    - Remote or Wearable Patient Monitoring Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/remote-or-wearable-patient-monitoring-devices-euas)
    - Respiratory Assist Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/respiratory-assist-devices-euas)
    - Ventilators and Ventilator Accessories EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/ventilators-and-ventilator-accessories-euas)
    - Other Medical Device EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/other-medical-device-euas)
  - Information About COVID-19 EUAs for Medical Devices

Vaccines

The HHS Secretary declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564 of the FD&C Act, effective March 27, 2020. The EUAs subsequently issued by FDA are listed in the table below this blue box.

- Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the FD&C Act (https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency) (February 4, 2020)
- Emergency Use Authorization Declaration (https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration) (March 27, 2020)

For additional information about COVID-19 vaccines, see:

- COVID-19 Vaccines (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines)
- Emergency Use Authorization for Vaccines Explained (/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained)

- Infographic: The Path for a COVID-19 Vaccine From Research to Emergency Use Authorization (https://www.fda.gov/media/143890/download) (PDF, 723 KB)
- Vaccine EUA Questions and Answers for Stakeholders (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/vaccine-eua-questions-and-answers-stakeholders)

Federal Register notices:

- Authorizations of Emergency Use of Two Biological Products During the COVID-19 Pandemic; Availability (https://www.federalregister.gov/documents/2021/01/19/2021-01022/authorizations-of-emergency-use-of-two-biological-products-during-the-covid-19-pandemic-availability)
    - On December 11, 2020, FDA issued an EUA to Pfizer, Inc. for the Pfizer-BioNTech COVID-19 Vaccine, subject to the terms of the Authorization. On December 18, 2020, FDA issued an EUA to ModernaTX, Inc. for the Moderna COVID-19 Vaccine, subject to the terms of the Authorization.

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Date of First EUA Issuance	Most Recent Letter of Authorization (PDF)	Authorized Use	Fact Sheets and Manufacturer Instructions/Package Insert (PDF)	Additional Information and Decision Memoranda (PDF)
+ 02/27/2021	Janssen COVID-19 Vaccine (https://www.fda.gov/media/146303/download) (371KB) (Reissued June 10 and October 20, 2021) Letter Granting EUA Amendment (March 29, 2021) (/media/147194/download) (152KB) Letter Granting EUA Amendment (April 23, 2021) (/media/147865/download) (229KB) Concurrence Letter (/media/150064/download) (June 10, 2021) (26KB) Concurrence Letter (/media/150136/download) (June 15, 2021) (57KB) Concurrence Letter (/media/150163/download) (June 16, 2021) (70KB) Concurrence Letter (/media/150567/download) (July 2, 2021) (317.7KB) Letter Granting EUA Amendment (July 12, 2021) (/media/150723/download) (210KB) Concurrence Letter (/media/150743/download) (July 13, 2021) (213KB) Concurrence Letter (/media/151141/download) (July 28, 2021) (63KB) Letter Granting EUA Amendment (August 30, 2021) (/media/151868/download) (80KB) Concurrence Letter (/media/152046/download) (September 8, 2021) (353KB) Concurrence Letter (/media/152171/download) (September 14, 2021) (253KB) Concurrence Letter (/media/152547/download) (September 29, 2021) (28KB) Concurrence Letter (/media/153931/download) (November 5, 2021) (212KB)	For the prevention of Coronavirus Disease 2019 (COVID-19) for individuals 18 years of age and older	Healthcare Providers (https://www.fda.gov/media/146304/download) (543KB) Recipients and Caregivers (https://www.fda.gov/media/146305/download) (279KB) • View the Fact Sheet for Recipients and Caregivers in multiple additional languages (https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine#translated)	More information about the Janssen COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine) Frequently Asked Questions on the Janssen COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine-frequently-asked-questions) COVID-19 Vaccine Expiration Dating Extensions (https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#covidvaccines) Decision Memorandum (/media/146338/download) (974KB, February 2021 initial EUA issuance) Decision Memorandum (/media/150081/download) (362KB, June 2021 EUA reissuance) Decision Memorandum Addendum (/media/150139/download) (59KB, June 2021 EUA reissuance) Decision Memorandum Addendum (/media/150571/download)(61KB, July 1, 2021 Assessment of Certain Janssen COVID-19 Vaccine Batches) Decision Memorandum Addendum (/media/150745/download) (58KB, July 13, 2021 Assessment of Certain Janssen COVID-19 Vaccine Batches)

		Most Recent Letter of Authorization (PDF)	Authorized Use	Fact Sheets and Manufacturer Instructions/Package Insert (PDF)	Additional Information and Decision Memoranda (PDF)
					Decision Memorandum Addendum (/media/152100/download) (60KB, September 8, 2021 Assessment of Certain Janssen COVID-19 Vaccine Batches) Decision Memorandum Addendum (/media/152170/download) (55KB, September 14, 2021 Assessment of Certain Janssen COVID-19 Vaccine Batches) Decision Memorandum Addendum (/media/152567/download) (57KB, September 29, 2021 Assessment of Certain Janssen COVID-19 Vaccine Batches) Decision Memorandum (/media/153441/download) (605KB, October 20, 2021 EUA reissuance) Memorandum to the File (/media/153439/download) (940KB, October 20, 2021 EUA amendment to support use of a Janssen COVID-19 Vaccine heterologous booster dose following primary vaccination with other authorized COVID-19 vaccines)
+	12/18/2020	Moderna COVID-19 Vaccine (/media/144636/download) (403KB) (Reissued February 25, July 7, August 12, and October 20, 2021) Letter Granting EUA Amendment (April 1, 2021) (/media/147284/download) (193KB) Letter Granting EUA Amendment (June 25, 2021) (/media/150387/download) (90KB) Letter Granting EUA Amendment (August 30, 2021) (/media/151855/download) (58KB)	For the prevention of Coronavirus Disease 2019 (COVID-19) for individuals 18 years of age and older	Healthcare Providers (/media/144637/download) (609KB) • Important prescribing information for vaccine providers on booster dose volume (0.25mL) and vial presentation (/media/153354/download) (230KB) (October 21, 2021) Recipients and Caregivers (/media/144638/download) (272KB) • View the Fact Sheet for Recipients and Caregivers in multiple additional languages (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine#translated)	More information about the Moderna COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine) Frequently Asked Questions on the Moderna COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine-frequently-asked-questions) Decision Memorandum (/media/144673/download) (769KB) Decision Memorandum (/media/151611/download) (65KB, August 12, 2021 EUA reissuance) Decision Memorandum (/media/153911/download) (606KB, October 20, 2021 EUA reissuance) Memorandum to the File (/media/153912/download) (605KB, October 20, 2021 EUA amendment to support use of a Moderna COVID-19 Vaccine heterologous booster dose following primary vaccination with other authorized COVID-19 vaccines)

Date of First EUA Issuance	Most Recent Letter of Authorization (PDF)	Authorized Use	Fact Sheets and Manufacturer Instructions/Package Insert (PDF)	Additional Information and Decision Memoranda (PDF)
+ 12/11/2020	Pfizer-BioNTech COVID-19 Vaccine (/media/150386/download) (428KB) (Reissued February 25, May 10, June 25, August 12, August 23, September 22, October 20, 2021, and October 29, 2021) Letter Granting EUA Amendment (January 6, 2021) (/media/144955/download) (164KB) Letter Granting EUA Amendment (January 22, 2021) (/media/145493/download) (190KB) Letter Granting EUA Amendment (April 6, 2021) (/media/147390/download) (166KB) Letter Granting EUA Amendment (May 19, 2021) (/media/148877/download) (184KB) Concurrence Letter (/media/151731/download) (August 22, 2021) (68KB)	For the prevention of 2019 coronavirus disease (COVID-19) in people 5 and older On August 23, 2021, FDA approved the Pfizer-BioNTech COVID-19 Vaccine, now known as Comirnaty, for the prevention of COVID-19.	Healthcare Providers (/media/153713/download) (1.33MB) – for 12 years of age and older, purple cap (must dilute) Healthcare Providers (/media/153715/download) (1.08MB) – for 12 years of age and older, gray cap (no dilution) - This formulation is not yet available in the United States. Healthcare Providers (/media/153714/download) (1.32MB) – for 5-11 years of age, orange cap (must dilute) Recipients and Caregivers (/media/153716/download) (225KB) –12 years of age and older Recipients and Caregivers (/media/153717/download) (221KB) – 5-11 years of age • View the Fact Sheet for Recipients and Caregivers in multiple additional languages (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine#translated)	More information about the Pfizer-BioNTech COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine) Frequently Asked Questions on the Pfizer-BioNTech COVID-19 Vaccine (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine-frequently-asked-questions) COVID-19 Vaccine Expiration Dating Extensions (https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#covidvaccines) Decision Memorandum (/media/144416/download) (709KB, December 2020 initial EUA issuance) Decision Memorandum (/media/148542/download) (868KB, May 2021 EUA reissuance) Decision Memorandum (/media/151613/download) (93KB, August 12, 2021 EUA reissuance) Decision Memorandum (/media/152432/download) (362KB, September 24, 2021) Decision Memorandum (/media/153482/download) (630KB, October 20, 2021 EUA reissuance)

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Drug and Biological Therapeutic Products

The HHS Secretary declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564 of the FD&C Act, effective March 27, 2020. The EUAs subsequently issued by FDA are listed in the table below this blue box.

- Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the FD&C Act (https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency) (February 4, 2020)
- Emergency Use Authorization Declaration (https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration) (March 27, 2020)

Related information: FDA Combating COVID-19 With Therapeutics (https://www.fda.gov/media/136832/download) (PDF, 610 KB)

COVID-19 EUA FAERS Public Dashboard

The dashboard provides weekly updates of adverse event reports submitted to FAERS for drugs and therapeutic biological products used under EUA during the COVID-19 public health emergency. After launching the FAERS Public Dashboard (/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard), click on the COVID-19 EUA link

at the top of the home page to open the COVID-19 EUA FAERS Public Dashboard.

Federal Register notices:

- Authorizations and Revocation of Emergency Use of Drugs During the COVID-19 Pandemic; Availability (https://www.federalregister.gov/documents/2020/09/11/2020-20041/authorizations-and-revocation-of-emergency-use-of-drugs-during-the-covid-19-pandemic-availability)
  - FDA announced issuance of four authorizations for the emergency use of drugs during the COVID-19 pandemic and one revocation. On March 28, 2020, FDA issued an EUA to BARDA for oral formulations of chloroquine phosphate and hydroxychloroquine sulfate, subject to the terms of the Authorization. On April 30, 2020, FDA issued an EUA to Fresenius Medical Care for multiFiltrate PRO System and multiBic/multiPlus Solutions, subject to the terms of the Authorization. On May 1, 2020, FDA issued an EUA to Gilead Sciences, Inc. for remdesivir, subject to the terms of the Authorization. On May 8, 2020, FDA issued an EUA to Fresenius Kabi USA, LLC for Fresenius Propoven 2% Emulsion, subject to the terms of the Authorization. FDA revoked the EUA for BARDA's oral formulations of chloroquine phosphate and hydroxychloroquine sulfate on March 28, 2020.
- Authorizations of Emergency Use of Certain Drug and Biological Products During the COVID-19 Pandemic; Availability (https://www.federalregister.gov/documents/2021/02/19/2021-03429/authorizations-of-emergency-use-of-certain-drug-and-biological-products-during-the-covid-19-pandemic)
  - FDA announced issuance of five authorizations for the emergency use of drug and biological products during the COVID-19 pandemic. On August 13, 2020, FDA issued an EUA to Baxter for REGIOCIT, subject to the terms of the Authorization. On August 23, 2020, FDA issued an EUA to ASPR/HHS for COVID-19 convalescent plasma, subject to the terms of the Authorization. On November 9, 2020, FDA issued an EUA to Eli Lilly and Company for bamlanivimab, subject to the terms of the Authorization (technical correction on November 10, 2020). On November 19, 2020, FDA issued an EUA to Eli Lilly and Company for OLUMIANT (baricitinib), for use in combination with VEKLURY (remdesivir), subject to the terms of the Authorization. On November 21, 2020, FDA issued an EUA to Regeneron Pharmaceuticals, Inc. for casirivimab and imdevimab, administered together, subject to the terms of the Authorization.
- Authorization and Revocation of Emergency Use of Drugs During the COVID-19 Pandemic; Availability (https://www.federalregister.gov/documents/2021/06/23/2021-13183/authorization-and-revocation-of-emergency-use-of-drugs-during-the-covid-19-pandemic-availability)
  - FDA announced the issuance of an EUA for a drug for use during the COVID-19 pandemic. FDA issued the Authorization under the Federal Food, Drug, and Cosmetic Act (FD&C Act), as requested by B. Braun Melsungen AG. The Authorization contains, among other things, conditions on the emergency use of the authorized drug. FDA also annouced the revocation of the Authorization issued to Eli Lilly and Company for bamlanivimab alone. FDA revoked this authorization on April 16, 2021. Reprinted in this document is the issuance of the Authorization and the revocation, which include an explanation of the reasons for issuance or revocation.
- Authorizations of Emergency Use of Certain Biological Products During the COVID-19 Pandemic; Availability (https://www.federalregister.gov/documents/2021/08/05/2021-16705/authorizations-of-emergency-use-of-certain-biological-products-during-the-covid-19-pandemic)
  - FDA announced the issuance of two authorizations for biological products for use during the COVID-19 pandemic. On May 26, 2021, FDA issued an EUA to GlaxoSmithKline LLC for sotrovimab, subject to the terms of the Authorization. On June 24, 2021, FDA issued an EUA to Genentech, Inc. for ACTEMRA (tocilizumab), subject to the terms of the Authorization.

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Date of First EUA Issuance	Most Recent Letter of Authorization (PDF)	Authorized Use [1]	Fact Sheets and Manufacturer Instructions/ Package Insert (PDF)

Date of First EUA Issuance	Most Recent Letter of Authorization (PDF)	Authorized Use [1]	Fact Sheets and Manufacturer Instructions/ Package Insert (PDF)
+ 06/24/2021	Actemra (Tocilizumab (/media/150319/download)) (107KB)	For the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).	Healthcare Providers (/media/150321/download) (231KB) Patients, Parents, and Caregivers (/media/150320/download) (47KB) Frequently Asked Questions on the Emergency Use Authorization of Actemra (Tocilizumab) (/media/150345/download) (128KB)
+ 05/26/2021	Sotrovimab (/media/149532/download) (388KB) (reissued October 8, 2021)	For the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.	Healthcare Providers (/media/149534/download) (424KB) (updated November 3, 2021) Patients, Parents, and Caregivers (/media/149533/download) (134KB) (updated November 3, 2021) Frequently Asked Questions on the Emergency Use Authorization of Sotrovimab (/media/149535/download) (288KB) (updated October 19, 2021) CDER Scientific Review Documents Supporting EUA (/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological)
+ 03/12/2021	Propofol-Lipuro 1% (/media/146680/download) (344KB)	To maintain sedation via continuous infusion in patients greater than age 16 with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting. [2]	Healthcare Providers (/media/146681/download) (420KB) Patients, Parents, and Caregivers (/media/146682/download) (172KB)
+ 02/09/2021	Bamlanivimab and Etesevimab (/media/145801/download) (488KB) (Reissued February 25, 2021, August 27, 2021 and September 16, 2021) Bamlanivimab and Etesevimab Authorized States, Territories, and US Jurisdictions (/media/151719/download) (116KB) (November 3, 2021)	Bamlanivimab and etesevimab administered together for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.	Healthcare Providers (/media/145802/download) (737KB) (updated September 16, 2021) Patients, Parents, and Caregivers (/media/145803/download) (157KB) (updated September 16, 2021) • Spanish (/media/148713/download) (158KB) (updated September 16, 2021) Dear Healthcare Provider Letter (/media/145804/download) (370KB) Statement on Post-Exposure Prophylaxis (/drugs/drug-safety-and-availability/fda-authorizes-bamlanivimab-and-etesevimab-monoclonal-antibody-therapy-post-exposure-prophylaxis) (September 16, 2021) Frequently Asked Questions on the Emergency Use Authorization for Bamlanivimab and Etesevimab (/media/145808/download) (342KB) (updated October 19, 2021) ASPR and FDA notices about (https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/May-26%2c-2021-Update.aspx)bamlanivimab/etesevimab (https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/default.aspx) CDER Scientific Review Documents Supporting EUA (/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological)

Date of First EUA Issuance	Most Recent Letter of Authorization (PDF)	Authorized Use [1]	Fact Sheets and Manufacturer Instructions/ Package Insert (PDF)
+ 11/21/2020	REGEN-COV (Casirivimab and Imdevimab) (/media/145610/download) (506KB) (Reissued February 3, 2021, February 25, 2021, June 3, 2021, July 30, 2021 and September 9, 2021)	Casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.	Healthcare Providers (/media/145611/download) (742KB) (updated November 1, 2021) • Spanish (/media/151403/download) (623KB) Patients, Parents, and Caregivers (/media/145612/download) (147KB) (updated July 30, 2021) • Spanish (/media/151404/download) (247KB) Dear Healthcare Provider Letter (/media/143901/download) (435KB) (updated September 16, 2021) Statement on Post-Exposure Prophylaxis (/drugs/drug-safety-and-availability/fda-authorizes-regen-cov-monoclonal-antibody-therapy-post-exposure-prophylaxis-prevention-covid-19) (July 30, 2021) Frequently Asked Questions on the Emergency Use Authorization of REGEN-COV (Casirivimab and Imdevimab) (/media/143894/download) (311KB) (updated October 19, 2021) CDER Scientific Review Documents Supporting EUA (/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological) Quick Reference Guide for Co-Packaged REGEN-COV (/media/152051/download) (38KB) (September 16, 2021)
+ 11/19/2020	Baricitinib (Olumiant) (/media/143822/download) (Revised July 28, 2021)	For emergency use by healthcare providers for the treatment COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).	Healthcare Providers (/media/143823/download) (Updated October 20, 2021)(155KB) Patients, Parents, and Caregivers (/media/143824/download) (Updated July 28, 2021) (55KB) Frequently Asked Questions on the Emergency Use Authorization for Olumiant (baricitinib) for Treatment COVID-19 (/media/143825/download) (270KB) (Updated July 28, 2021) CDER Scientific Review Documents Supporting EUA (/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological)
+ 08/23/2020	COVID-19 convalescent plasma (/media/141477/download) (285KB) (Reissued February 23, 2021 and March 9, 2021) Letter Granting EUA Amendment (/media/149803/download) (June 2, 2021) (107KB)	For the treatment of hospitalized patients with Coronavirus Disease 2019 (COVID-19)	Healthcare Providers (/media/141478/download) (176KB) Patients and Parents/ Caregivers (/media/141479/download) (124KB) Decision Memorandum (/media/141480/download) (166KB)
+ 08/13/2020	REGIOCIT replacement solution that contains citrate for regional citrate anticoagulation (RCA) of the extracorporeal circuit (/media/141168/download) (92KB)	To be used as a replacement solution only in adult patients treated with continuous renal replacement therapy (CRRT), and for whom regional citrate anticoagulation is appropriate, in a critical care setting	Healthcare Providers (/media/141170/download) (108KB) Patients and Caregivers (/media/141172/download) (52KB) REGIOCIT package insert for EUA (/media/141186/download) (140KB)
+ 05/08/2020	Fresenius Kabi Propoven 2% (/media/137888/download) (209KB)	To maintain sedation via continuous infusion in patients older than age 16 with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting [2]	Healthcare Providers (/media/137889/download) (288KB) Patients and Parent/Caregivers (/media/137890/download) (39KB) Propoven 2% Wall Chart (/media/137891/download) (2.4MB)

Date of First EUA Issuance	Most Recent Letter of Authorization (PDF)	Authorized Use [1]	Fact Sheets and Manufacturer Instructions/ Package Insert (PDF)
+ 05/01/2020	Remdesivir for Certain Hospitalized COVID-19 Patients (/media/137564/download) (423KB) (Reissued August 28, 2020, October 1, 2020, and October 22, 2020)	For emergency use by licensed healthcare providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. On October 22, 2020, FDA approved Veklury (remdesivir) (/news-events/press-announcements/fda-approves-first-treatment-covid-19) for use in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care. This approval does not include the entire population that had been authorized to use Veklury under an Emergency Use Authorization (EUA) originally issued on May 1, 2020. In order to ensure continued access to the pediatric population previously covered under the EUA, the EUA for Veklury continues to authorize Veklury for emergency use by licensed healthcare providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. For additional information, also see: FDA's approval of Veklury (remdesivir) for the treatment of COVID-19—The Science of Safety and Effectiveness (/drugs/news-events-human-drugs/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness)	Healthcare Providers (/media/137566/download) (375KB) Patients and Parent/ Caregivers (/media/137565/download) (94KB) • Spanish (/media/139460/download) (563KB) Frequently Asked Questions on the EUA for Veklury (remdesivir) for Certain Hospitalized Patients (/media/137574/download) (194KB) (Updated February 4, 2021) • Spanish (/media/138804/download) (195KB)

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[1] The virus that causes COVID-19 has led to an increased number of patients requiring critical care, such as with severe respiratory illness. As a result, there is a shortage of adequate, FDA-approved drugs used for their treatment, such as propofol for sedation of mechanically ventilated patients.

[2] In the circumstances of this public health emergency, it would not be feasible to require healthcare providers to seek to limit Fresenius Propoven 2% Emulsion or Propofol-Lipuro 1% only to be used for patients with suspected or confirmed COVID-19; therefore, this authorization does not limit use to such patients.

[3] The multiBic/multiPlus Solutions include multiBic dialysate and replacement fluid and multiPlus dialysate. The multiBic replacement fluid is regulated as a drug by CDER. The multiFiltrate PRO System, multiBic dialysate and the multiPlus dialysate solutions are regulated as devices by CDRH.

Information About COVID-19 EUAs for Medical Devices

Information about COVID-19 EUAs for medical devices can be found below and at: Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices (/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices).

On February 4, 2020 (https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency), the Secretary determined pursuant to section 564 of the FD&C Act that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad and that involves a novel (new) coronavirus (nCoV) first detected in Wuhan City, Hubei Province, China in 2019 (2019-nCoV).

On the basis of this determination, the HHS Secretary issued three declarations related to medical devices:

- Determination of Public Health Emergency (https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency) (effective February 4, 2020), and declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19
- Emergency Use Declaration (https://www.federalregister.gov/documents/2020/03/10/2020-04823/emergency-use-declaration) (effective March 2, 2020), that circumstances exist justifying the authorization of emergency use of personal respiratory protective devices during the COVID-19 outbreak
- Emergency Use Authorization Declaration (https://www.federalregister.gov/documents/2020/03/27/2020-06541/emergency-use-authorization-declaration) (effective March 24, 2020), that circumstances exist justifying the authorization of emergency use of medical devices, including alternative products used as medical devices, due to shortages during the COVID-19 outbreak

For identification of the applicable declaration for each EUA, please see each EUA letter of authorization and/or the corresponding Federal Register notice.

Related information: FDA Combating COVID-19 With Medical Devices (https://www.fda.gov/media/136702/download) (PDF, 708 KB)

In Vitro Diagnostics

Please see the page In Vitro Diagnostics EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas) for information about in vitro diagnostics EUAs, including templates.

For current SARS-CoV-2 in vitro diagnostic EUAs, see:

- Molecular Diagnostic Tests for SARS-CoV-2 (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2)
- Antigen Diagnostic Tests for SARS-CoV-2 (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2)
- Serology and Other Adaptive Immune Response Tests for SARS-CoV-2 (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-serology-and-other-adaptive-immune-response-tests-sars-cov-2)
- IVDs for Management of COVID-19 Patients (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-ivds-management-covid-19-patients)

On February 29, 2020, the FDA issued an immediately in effect guidance (/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised) with policy specific to development of in vitro diagnostic tests during this public health emergency. This guidance was updated on March 16, 2020, May 4, 2020, and May 11, 2020.

CDC has granted a right of reference to the performance data contained in CDC's EUA (FDA submission number EUA200001) to any entity seeking an FDA EUA for a COVID-19 diagnostic device.

Templates for these EUA submissions (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas) are available to help facilitate the preparation, submission, and authorization of an EUA.

For additional information, see FAQs on Diagnostic Testing for SARS-CoV-2 (/medical-devices/coronavirus-covid-19-and-medical-devices/faqs-testing-sars-cov-2), EUA Authorized Serology Test Performance (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance), and CLIA and University Laboratory Testing FAQ (https://www.cms.gov/files/document/clia-university-lab-testing.pdf) (CMS).

Molecular SARS-CoV-2 Diagnostic Tests for COVID-19 that have been granted a De Novo, 510(k) clearance or PMA

BioFire Respiratory Panel 2.1 (RP2.1) - On March 17, 2021, FDA granted the first marketing authorization using the De Novo review pathway for the BioFire Respiratory Panel 2.1 (RP2.1) (https://www.accessdata.fda.gov/cdrh_docs/pdf20/DEN200031.pdf) (PDF, 630 KB). The BioFire RP2.1 is for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections, including COVID-19. *Also see the FDA news release: FDA Permits Marketing of First SARS-CoV-2 Diagnostic Test Using Traditional Premarket Review Process (/news-events/press-announcements/fda-permits-marketing-first-sars-cov-2-diagnostic-test-using-traditional-premarket-review-process). With granting of the De Novo for the BioFire RP2.1, the FDA revoked the EUA (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information) for this device, which was initially authorized for emergency use in May 2020.*

The BioFire Respiratory Panel 2.1 (RP2.1) was reviewed under the De Novo premarket review pathway (/medical-devices/premarket-submissions/de-novo-classification-request), a regulatory pathway for low-to-moderate-risk devices of a new type. Along with this De Novo authorization, the FDA is establishing criteria, called special controls, that define the requirements related to labeling and performance testing. When met, the special controls, in combination with general controls, provide a reasonable assurance of safety and effectiveness for tests of this type. This action also creates a new regulatory classification, which means that subsequent devices of the same type with the same intended use may go through the FDA's 510(k) pathway, whereby devices can obtain clearance by demonstrating substantial equivalence to a predicate device.

Personal Protective Equipment (PPE)

Please see the page Personal Protective Equipment EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/personal-protective-equipment-euas) for current EUAs.

For additional information, see Recent Final Medical Device Guidance Documents (/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/recent-final-medical-device-guidance-documents), and Non-NIOSH Approved Respirator FAQ (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/faqs-euas-non-niosh-approved-respirators-during-covid-19-pandemic).

See Revoked EUAs for Non-NIOSH-Approved Disposable Filtering Facepiece Respirators and Decontamination and Bioburden Reduction Systems below for information about June 30, 2021 EUA revocations.

Other Medical Device EUAs

Please see the following pages for EUA templates and additional information about other types of medical device EUAs for COVID-19:

- Blood Purification Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/blood-purification-devices-euas)
- Continuous Renal Replacement Therapy and Hemodialysis Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/continuous-renal-replacement-therapy-and-hemodialysis-devices-euas)
- Infusion Pump EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/infusion-pump-euas)
- Remote or Wearable Patient Monitoring Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/remote-or-wearable-patient-monitoring-devices-euas)
- Respiratory Assist Devices EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/respiratory-assist-devices-euas)
- Ventilators and Ventilator Accessories EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/ventilators-and-ventilator-accessories-euas)
- Other Medical Device EUAs (/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/other-medical-device-euas)

Revoked EUAs for Non-NIOSH-Approved Disposable Filtering Facepiece Respirators (FFRs) and Decontamination and Bioburden Reduction Systems

On June 30, 2021, the FDA announced (/news-events/press-announcements/fda-brief-fda-revokes-emergency-use-authorizations-certain-respirators-and-decontamination-systems)the revocation of the following EUAs:

- Imported, Non-NIOSH-Approved Disposable Filtering Facepiece Respirators (https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/revoked-euas-non-niosh-approved-disposable-filtering-facepiece-respirators#imported)(effective July 6, 2021)
- Non-NIOSH-Approved Disposable Filtering Facepiece Respirators Manufactured in China (https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/revoked-euas-non-niosh-approved-disposable-filtering-facepiece-respirators#china) (effective July 6, 2021)
- Decontamination and Bioburden Reduction System EUAs for Personal Protective Equipment (https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/historical-information-about-device-emergency-use-authorizations#decontamination) (effective June 30, 2021)

As of the effective date of the revocations, these devices will no longer be authorized for use by health care personnel in health care settings.

For additional information, please see Update: FDA No Longer Authorizes Use of Non-NIOSH-Approved or Decontaminated Disposable Respirators - Letter to Health Care Personnel and Facilities (/medical-devices/letters-health-care-providers/update-fda-no-longer-authorizes-use-non-niosh-approved-or-decontaminated-disposable-respirators).
Historical information regarding these EUAs can be found on Historical Information about Device Emergency Use Authorizations (/medical-devices/emergency-use-authorizations-medical-devices/historical-information-about-device-emergency-use-authorizations) and Emergency Use Authorization--Archived Information (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information).

Medical Device Federal Register notices

- Authorization of Emergency Use of Certain Medical Devices During COVID-19; Availability (https://www.federalregister.gov/documents/2020/06/05/2020-12117/authorization-of-emergency-use-of-certain-medical-devices-during-covid-19-availability) (through April 10, 2020)
- Authorization of Emergency Use of Certain Medical Devices During COVID-19; Availability (https://www.federalregister.gov/documents/2020/07/14/2020-15137/authorization-of-emergency-use-of-certain-medical-devices-during-covid-19-availability) (April 11, 2020- May 15, 2020)
- Authorization of Emergency Use of Certain Medical Devices During COVID-19; Availability (https://www.federalregister.gov/documents/2020/11/20/2020-25603/authorization-of-emergency-use-of-certain-medical-devices-during-covid-19-availability) (May 15, 2020- September 14, 2020)
- Authorization of Emergency Use of Certain Medical Devices During COVID-19; Availability (https://www.federalregister.gov/documents/2021/04/23/2021-08467/authorization-of-emergency-use-of-certain-medical-devices-during-covid-19-availability) (September 15, 2020 - February 15, 2021)
- Authorization of Emergency Use of Certain Medical Devices During COVID-19; Availability (https://www.federalregister.gov/documents/2021/07/23/2021-15680/authorization-of-emergency-use-of-certain-medical-devices-during-covid-19-availability)(February 16, 2021- May 31, 2021)
- Authorization of Emergency Use of Certain Medical Devices During COVID-19; Availability (https://www.federalregister.gov/documents/2021/10/28/2021-23501/authorization-of-emergency-use-of-certain-medical-devices-during-covid-19-availability) (June 1, 2021 - September 10, 2021)
- Revocation notices for EUAs are made available on the EUA archive page (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information)

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Other Current EUAs

The tables below provide information on current EUAs:

- Anthrax EUAs
- Ebola Virus EUA Information
- Enterovirus D68 (EV-D68) EUA Information
- Freeze Dried Plasma Information
- H7N9 Influenza EUA Information
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV) EUA Information
- Nerve Agent EUA Information
- Zika Virus EUA Information

Information about EUAs that are no longer in effect is available on our EUA archive page (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information).

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Anthrax EUAs

The 2016 FDA Doxycycline Emergency Dispensing Order (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-dispensing-orders#doxy) and CDC Doxycycline Emergency Use Instructions (EUI) (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-dispensing-orders#doxy) together replace the need for the doxycycline mass dispensing EUA (issued on July 21, 2011). Therefore, the doxycycline emergency dispensing order and EUI should be used by stakeholders for anthrax preparedness and response instead of the mass dispensing EUA.

The July 21, 2011, doxycycline mass dispensing EUA, and the October 14, 2011, National Postal Model anthrax EUA will be terminated by FDA, and notice of such termination will be published in the *Federal Register*. For additional information, see Emergency Use Authorization--Archived Information (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information).

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Ebola Virus EUA Information

Ebola preparedness and response updates from FDA (/emergency-preparedness-and-response/mcm-issues/ebola-preparedness-and-response-updates-fda) (all agency activities)

For more information about the diagnostics below, also see Emergency Use Authorizations (/about-fda/page-not-found) **(current device EUAs).**

Ebola Diagnostic Tests with De Novo, 510(k) or PMA

- **OraQuickEbola Rapid Antigen Test** (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN190025)- On October 10, 2019, FDA allowed marketing (https://www.accessdata.fda.gov/cdrh_docs/pdf19/DEN190025.pdf) (PDF, 255 KB) of a rapid diagnostic test (RDT) to detect Ebola virus antigens (proteins) in human blood from certain living individuals and samples from certain recently deceased individuals suspected to have died from Ebola (cadaveric oral fluid). The OraQuick Ebola Rapid Antigen Test is the first rapid diagnostic test the FDA has allowed to be marketed in the U.S. for Ebola virus disease (EVD). The test provides a rapid, presumptive diagnosis that must be confirmed. *Also see the FDA news release: FDA allows marketing of first rapid diagnostic test for detecting Ebola virus antigens (/news-events/press-announcements/fda-allows-marketing-first-rapid-diagnostic-test-detecting-ebola-virus-antigens)*

  The OraQuick Ebola Test was reviewed under the De Novo premarket review pathway (/medical-devices/premarket-submissions/de-novo-classification-request), a regulatory pathway for low-to-moderate-risk devices of a new type. Along with this marketing authorization, the FDA is establishing criteria, called special controls, that determine the requirements for demonstrating accuracy, reliability and effectiveness of tests intended to identify Ebola virus antigens. These special controls, when met along with general controls, provide a reasonable assurance of safety and effectiveness for tests of this type. This action also creates a new regulatory classification, which means that subsequent devices of the same type with the same intended use may go through the FDA's 510(k) pathway, whereby devices can obtain clearance by demonstrating substantial equivalence to a predicate device.

Medical Product	Date of EUA Issuance	Letter of Authorization	Federal Register Notice for EUA	Fact Sheets and Manufacturer Instructions/Package Insert	E
EZ1 Real-time RT-PCR Assay (DoD)	August 5, 2014 (initial issuance) October 10, 2014 (reissuance)	Authorization (/media/89984/download) (PDF, 61 KB)	FR notice (https://www.federalregister.gov/articles/2014/09/17/2014-22086/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-ebola-zaire-virus)	• Healthcare (/media/89986/download) (PDF, 58 KB) • Patients (/media/89988/download) (PDF, 59 KB) • Instruction Booklet (/media/89989/download) (PDF, 1.1 MB)	D D (h 1 d
CDC Ebola Virus NP Real-time RT-PCR Assay (CDC)	October 10, 2014 (initial issuance) March 2, 2015 (reissuance) October 8, 2019 (amended)	Authorization (/media/91083/download) (PDF, 282 KB) Letter granting EUA amendment(s) (PDF, 134 KB) (/media/131606/download)	FR notice (https://www.federalregister.gov/articles/2014/12/24/2014-30108/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-ebola-zaire-virus)	• Healthcare (/media/91087/download) (PDF, 207 KB) • Patients (/media/91092/download) (PDF, 149 KB) • Instructions for Use (/media/91097/download) (PDF, 496 KB)	D D (h 1 d
CDC Ebola Virus VP40 Real-time RT-PCR Assay (CDC)	October 10, 2014 (initial issuance) March 2, 2015 (reissuance) October 8, 2019 (amended)	Authorization (/media/91105/download) (PDF, 285 KB) Letter granting EUA amendment(s) (PDF, 135 KB) (/media/131605/download)	FR notice (https://www.federalregister.gov/articles/2014/12/24/2014-30108/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-ebola-zaire-virus)	• Healthcare (/media/91111/download) (PDF, 207 KB) • Patients (/media/91118/download) (PDF, 149 KB) • Instructions for Use (/media/91142/download) (PDF, 494 KB)	D D (h 1 d
FilmArray NGDS BT-E Assay (Biofire Defense, LLC)	October 25, 2014 (initial issuance) March 2, 2015 (reissuance)	Authorization (/media/91070/download) (PDF, 326 KB)	FR notice (https://www.federalregister.gov/articles/2015/02/09/2015-02467/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-ebola-virus)	• Healthcare (/media/91149/download) (PDF, 40 KB) • Patients (/media/91153/download) (PDF, 40 KB) • Instructions for Use (/media/91077/download) (PDF, 740 KB)	D D (h 1 d
FilmArray Biothreat-E test (Biofire Defense, LLC)	October 25, 2014 November 12, 2019 (amended)	Authorization (/media/89580/download) (PDF, 73 KB) Letter granting EUA amendment(s) (PDF, 152 KB) (/media/132517/download)	FR notice (https://www.federalregister.gov/articles/2015/02/09/2015-02467/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-ebola-virus)	• Healthcare (/media/89585/download) (PDF, 227 KB) • Patients (/media/89604/download) (PDF, 191 KB) • Instructions for Use (/media/89614/download) (PDF, 1.6 MB)	D D (h 1 d
RealStar Ebolavirus RT-PCR Kit 1.0 (altona Diagnostics, GmbH)	November 10, 2014 (initial issuance) November 26, 2014 (reissuance)	Authorization (/media/123410/download) (PDF, 263 KB)	FR notice (https://www.federalregister.gov/articles/2015/02/09/2015-02467/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-ebola-virus)	• Healthcare (/media/120428/download) (PDF, 81 KB) • Patients (/media/120429/download) (PDF, 92 KB) • Instructions for Use (/media/120430/download) (PDF, 797 KB)	D D (h 1 d

LightMix Ebola Zaire rRT-PCR Test (Roche Molecular Systems, Inc.)	December 23, 2014	Authorization (/media/120431/download) (PDF, 2.2 MB)	FR notice (https://www.federalregister.gov/articles/2015/03/17/2015-06039/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-ebola-zaire-virus)	• Healthcare (/media/120432/download) (PDF, 59 KB) • Patients (/media/120433/download) (PDF, 60 KB) • Instructions for Use (/about-fda/page-not-found) (PDF, 328 KB)	D D (h 1 d
Xpert Ebola Assay (Cepheid)	March 23, 2015	Authorization (/media/91315/download) (PDF, 240 KB)	FR notice (https://www.federalregister.gov/articles/2015/06/05/2015-13699/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-ebola-virus)	• Healthcare (/media/91934/download) (PDF, 310 KB) • Patients (/media/91939/download) (PDF, 211 KB) • Instructions for Use (/media/91944/download) (PDF, 625 KB)	D D (h 1 d
Idylla Ebola Virus Triage Test (Biocartis NV)	May 26, 2016	Authorization (/media/98460/download) (PDF, 321 KB)	FR notice (https://www.federalregister.gov/articles/2016/07/08/2016-16176/authorizations-of-emergency-use-in-vitro-diagnostic-device-for-detection-of-ebola-zaire-virus)	• Healthcare (/media/98451/download)(PDF, 203 KB) • Patients (/media/98442/download) (PDF, 163 KB) • Instructions for Use (/media/98434/download) (PDF, 2.1 MB)	D D (h 1 d
DPP Ebola Antigen System (Chembio Diagnostic Systems, Inc.)	November 9, 2018 April 2, 2019 (amended)	Authorization (/media/117735/download) (PDF, 103 KB) Letter Granting EUA Amendment(s) (/media/122553/download) (PDF, 87 KB)	FR notice (https://www.federalregister.gov/documents/2019/02/13/2019-02134/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-ebola-virus)	• Healthcare (/media/117736/download)(PDF, 122 KB) • Patients (/media/117737/download) (PDF, 119 KB) • Instructions for Use (/media/117738/download) (PDF, 2 MB)	D D (h 1 d

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Enterovirus D68 (EV-D68) EUA Information

For more information about the diagnostics below, also see Emergency Use Authorizations (/about-fda/page-not-found) (current device EUAs).

Medical Product	Date of EUA Issuance	Letter of Authorization	Federal Register Notice for EUA	Fact Sheets and Manufacturer Instructions/Package Insert	EUA Determination and De
CDC Enterovirus D68 2014 Real-time RT-PCR Assay (EV-D68 2014 rRT-PCR)	May 12, 2015	Authorization (/media/120425/download) (PDF, 229 KB)	FR notice (https://www.federalregister.gov/articles/2015/07/01/2015-16125/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-enterovirus-d68)	• Healthcare (/media/92008/download) (PDF, 214 KB) • Patients (/media/120426/download) (PDF, 150 KB) • Instructions for Use (/media/120427/download)(PDF, 531 KB)	Determination and Declarat New *In Vitro* Diagnostics fo (https://www.federalregiste 04121/determination-and-c use-of-new-in-vitro-diagnos 2015)

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Freeze Dried Plasma Information

Also see FDA News Release: FDA takes action to support American military personnel by granting an authorization for freeze-dried plasma product to enable broader access while the agency works toward approval of the product (/news-events/press-announcements/fda-takes-action-support-american-military-personnel-granting-authorization-freeze-dried-plasma) (July 10, 2018)

Medical Product	Date of EUA Issuance	Letter of Authorization	Federal Register Notice for EUA	Fact Sheets and Manufacturer Instructions/Package Insert	EUA Determination and
Pathogen-Reduced Leukocyte-Depleted Freeze Dried Plasma (Centre de Transfusion Sanguine des Armées)	July 9, 2018 (initial issuance) May 8, 2020 (amendment)	Authorization (/media/114282/download) (PDF, 203 KB) Letter granting EUA amendments (/media/137970/download) (PDF, 60 KB)	FR notice (https://www.federalregister.gov/documents/2018/08/13/2018-17303/authorization-of-emergency-use-of-a-freeze-dried-plasma-treatment-for-hemorrhage-or-coagulopathy)	• Fact Sheet for U.S. Military Medical Personnel (/media/119949/download) (PDF, 132 KB) • Fact Sheet for Recipients (/media/119948/download) (PDF, 101 KB)	Determination by DoD (Declaration Regarding E Hemorrhage or Coagulo Agents of Military Com (https://www.federalreg 16331/emergency-use-o hemorrhage-due-to-age 9, 2018)

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H7N9 Influenza EUA Information

For more information about the diagnostics below, also see Emergency Use Authorizations (/about-fda/page-not-found) (current device EUAs).

Medical Product	Date of EUA Issuance	Letter of Authorization	Federal Register Notice for EUA	Fact Sheet and Manufacturer Instructions/Package Insert	EUA Determination and Declarat
CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay	April 22, 2013 (initial issuance) March 27, 2018 (reissuance)	Authorization (/media/85910/download) (PDF, 301 KB), re-issued March 27, 2018	FR notice (https://www.federalregister.gov/articles/2013/06/25/2013-15096/authorization-of-emergency-use-of-an-in-vitro-diagnostic-for-detection-of-the-novel-avian-influenza)	• Healthcare (/media/85915/download) (PDF, 46 KB) • Patients (/media/85446/download) (PDF, 32 KB) • Instructions for Use (/media/85454/download) (PDF, 433 KB)	Determination and Declaration R Diagnostics for Detection of the (https://www.federalregister.gov 10055/determination-and-declar vitro-diagnostics-for-detection-o Additional information from HHS (http://www.phe.gov/emergency influenza-virus.aspx)
Quidel Lyra Influenza A Subtype H7N9 Assay	February 14, 2014	Authorization (/media/87767/download) (PDF, 57 KB)	FR notice (https://www.federalregister.gov/articles/2014/04/17/2014-08706/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-novel-influenza-a)	• Healthcare (/media/87775/download) (PDF, 42 KB) • Patients (/media/87780/download) (PDF, 40 KB)	Determination and Declaration R Diagnostics for Detection of the (https://www.federalregister.gov 10055/determination-and-declar vitro-diagnostics-for-detection-o Additional information from HHS (http://www.phe.gov/emergency influenza-virus.aspx)

A/H7N9 Influenza Rapid Test	April 25, 2014	Authorization (/medical-devices/emergency-situations-medical-devices/ah7n9-influenza-rapid-test-letter-authorization)	FR notice (https://www.federalregister.gov/articles/2014/06/23/2014-14547/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-novel-influenza-a)	• Healthcare (/medical-devices/emergency-situations-medical-devices/fact-sheet-health-care-providers-interpreting-ah7n9-influenza-rapid-test-results) • Patients (/medical-devices/emergency-situations-medical-devices/fact-sheet-patients-understanding-results-ah7n9-influenza-rapid-test)	Determination and Declaration R Diagnostics for Detection of the (https://www.federalregister.gov 10055/determination-and-declar vitro-diagnostics-for-detection-o Additional information from HHS (http://www.phe.gov/emergency influenza-virus.aspx)

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Middle East Respiratory Syndrome Coronavirus (MERS-CoV) EUA Information

For more information about the diagnostics below, also see Emergency Use Authorizations (/about-fda/page-not-found) (current device EUAs).

Medical Product	Date of EUA Issuance	Letter of Authorization	Federal Register Notice for EUA	Fact Sheets and Manufacturer Instructions/Package Insert	EUA Determination
CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	June 5, 2013 (initial issuance) June 10, 2014 (reissuance)	Authorization (/media/88518/download) (PDF, 2.2 MB)	FR notice (https://www.federalregister.gov/documents/2013/07/17/2013-17103/authorization-of-emergency-use-of-an-in-vitro-diagnostic-for-detection-of-middle-east-respiratory)	• Healthcare (/medical-devices/emergency-situations-medical-devices/fact-sheet-health-care-professionals-interpreting-cdc-novel-coronavirus-2012-real-time-rt-pcr-assay) • Patients (/medical-devices/emergency-situations-medical-devices/fact-sheet-patients-understanding-results-cdc-novel-coronavirus-2012-real-time-rt-pcr-assay) • Contacts (/media/88505/download) (PDF, 1.2 MB) • Instructions for Use (/media/85951/download) (PDF, 743 KB)	Determination and D Diagnostics for Dete Coronavirus (MERS- (https://www.federa 13333/determinatio vitro-diagnostics-for Additional informati (http://www.phe.gov cov.aspx)
RealStar MERS-CoV RT-PCR Kit U.S.	July 17, 2015 (initial issuance) February 12, 2016 (reissuance)	Authorization (/media/93040/download) (PDF, 238 KB)	FR notice (https://www.federalregister.gov/documents/2015/09/01/2015-21585/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-middle-east)	• Healthcare (/media/93048/download) (PDF, 269 KB) • Patients (/media/93056/download) (PDF, 241 KB) • Instructions for Use (/media/120434/download) (PDF, 1.28 MB) • Fact Sheet for Asymptomatic Individuals Suspected of Exposure to MERS-CoV Cases (/media/95614/download) (PDF, 285 KB)	Determination and D Diagnostics for Dete Coronavirus (MERS- (https://www.federa 13333/determinatio vitro-diagnostics-for Additional informati (http://www.phe.gov cov.aspx)

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Nerve Agent EUA Information

On July 9, 2018, FDA approved (https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/212319Orig1s000ltr.pdf) (PDF, 49 KB) the 2 mg Atropine Auto-Injector manufactured by Rafa Laboratories, Ltd., for the treatment of poisoning by susceptible organophosphorous nerve agents having cholinesterase activity as well as organophosphorous or carbamate insecticides in adults and pediatric patients weighing over 90 lbs [41 kg] (generally over 10 years of age). For more information about the approved 2 mg Rafa Atropine Auto-Injector, see the product label (https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/212319s000lbl.pdf) (PDF, 482 KB). The EUA detailed in the table below is still in effect.

Medical Product	Date of EUA Issuance	Letter of Authorization	Federal Register Notice for EUA	Fact Sheets and Manufacturer Instructions/Package Insert	EUA Determination and D
Atropine Auto-Injector (Rafa Laboratories Ltd.)	April 11, 2017 (initial issuance) May 23, 2017 (amended) January 24, 2018 (amended) March 6, 2018 (amended) May 15, 2018 (amended)	Letter of Authorization (/media/104550/download) (PDF, 514 KB) Letter granting EUA amendment(s) (/media/105590/download) (PDF, 28 KB) 2nd letter granting EUA amendment(s) (/media/110881/download) (PDF, 33 KB) 3rd letter granting EUA amendment(s) (/media/111656/download) (PDF, 85 KB) 4th letter granting EUA amendment(s) (/media/113102/download) (PDF, 42 KB)	FR notice (https://www.federalregister.gov/documents/2017/06/30/2017-13664/emergency-use-authorizations-injectable-treatment-for-nerve-agent-or-certain-insecticide)	• Healthcare (/media/104559/download) (PDF, 531 KB) • Patients and Caregivers (/media/104564/download) (PDF, 675 KB)	Determination and Declar Certain Insecticide (Orgar Poisoning (https://www.federalregis 07685/determination-and of-injectable-treatments-f

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Zika Virus EUA Information

Zika virus response updates from FDA (/emergency-preparedness-and-response/mcm-issues/zika-virus-response-updates-fda)

Zika virus diagnostic development information (/emergency-preparedness-and-response/mcm-issues/zika-virus-diagnostic-development)

For more information about the diagnostics below, also see Emergency Use Authorizations (/about-fda/page-not-found) (current device EUAs).

Draft EUA review templates for Zika are available by email request to: CDRH-ZIKA-Templates@fda.hhs.gov (mailto:CDRH-ZIKA-Templates@fda.hhs.gov?Subject=EUA template request)

Laboratory personnel using Zika diagnostic assays under EUA are encouraged to report performance concerns directly to FDA at CDRH-EUA-Reporting@fda.hhs.gov (mailto:CDRH-EUA-Reporting@fda.hhs.gov), in addition to reporting concerns to the manufacturer.

Zika Diagnostic Tests with De Novo, 510(k), or PMA

- **ZIKV Detect 2.0 IgM Capture ELISA (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN180069)** - On May 23, 2019, FDA authorized marketing (https://www.accessdata.fda.gov/cdrh_docs/pdf18/DEN180069.pdf) (PDF, 175 KB) of the ZIKV Detect 2.0 IgM Capture

ELISA to detect Zika virus immunoglobulin (IgM) antibodies in human blood. The ZIKV Detect 2.0 IgM Capture ELISA is the first Zika diagnostic test the FDA has allowed to be marketed in the U.S.; previously, tests for detecting Zika virus IgM antibodies—including the ZIKV Detect 2.0 IgM Capture ELISA —had been authorized only for emergency use under the FDA's EUA authority. *Also see the FDA news release: FDA authorizes marketing of first diagnostic test for detecting Zika virus antibodies (/news-events/press-announcements/fda-authorizes-marketing-first-diagnostic-test-detecting-zika-virus-antibodies)*

- **ADVIA Centaur Zika test** (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K191578) – On July 17, 2019, FDA cleared the ADVIA Centaur Zika test. This is the second Zika diagnostic test FDA has allowed to be marketed in the U.S. for detecting Zika virus IgM antibodies. Previously, the test had been authorized only for emergency use under FDA's EUA authority.
- **LIAISON XL Zika Capture IgM Assay II** (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K192046) – On October 28, 2019, FDA cleared the LIAISON XL Zika Capture IgM Assay II for detecting Zika virus IgM antibodies. Previously, the test had been authorized only for emergency use under FDA's EUA authority.
- DPP Zika IgM Assay System (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K192046) – On June 3, 2020, FDA cleared a similar DPP Zika IgM System for detecting Zika virus IgM antibodies. Previously, the test had been authorized only for emergency use under FDA's EUA authority.

Medical Product	Date of EUA Issuance	Letters	Federal Register Notice for EUA	F I
CDC Zika Immunoglobulin M (IgM) Antibody Capture Enzyme-Linked Immunosorbent Assay *CDC statement on this EUA (http://www.cdc.gov/media/releases/2016/s0226-laboratory-test-for-zika-virus.html)*	February 26, 2016 (initial issuance) June 29, 2016 (amended) November 15, 2016 (amended) December 6, 2016 (amended) May 3, 2017 (amended) July 31, 2017 (amended) April 16, 2018 (amended) September 26, 2018 (amended)	Letter granting EUA amendment(s) (/media/101616/download) (PDF, 155 KB) Letter granting EUA amendment(s) (/media/101586/download) (PDF, 123 KB) Letter granting EUA amendment(s) (/media/120186/download) (PDF, 110 KB) Letter granting EUA amendment(s) (/media/120187/download) (PDF, 113 KB) Letter granting EUA amendment(s) (/media/120188/download) (PDF, 131 KB) Letter granting EUA amendment(s) (/media/120189/download) (PDF, 131 KB)	FR notice (https://www.federalregister.gov/articles/2016/03/28/2016-06888/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-diagnosis-of-zika-virus)	
CDC Trioplex Real-time RT-PCR Assay (Trioplex rRT-PCR) *CDC statement on this EUA (http://www.cdc.gov/media/releases/2016/s0318-zika-lab-test.html)*	March 17, 2016 (initial issuance) September 21, 2016 (amended) January 12, 2017 (amended) February 28, 2017 (amended) April 6, 2017 (amended) February 26, 2021 (amended)	Authorization (/media/96683/download) (PDF, 82 KB) Letter granting EUA amendment(s) (/media/100200/download) (PDF, 223 KB) Letter granting EUA amendment(s) (/media/102439/download) (PDF, 223 KB) Letter granting EUA amendment(s) (/media/103400/download) (PDF, 223 KB) Letter granting EUA amendment(s) (/media/120192/download) (PDF, 126 KB) Letter granting EUA amendment(s) (https://www.fda.gov/media/146320/download) (PDF, 143 KB)	FR notice (https://www.federalregister.gov/articles/2016/04/22/2016-09370/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-zika-virus)	

Zika Virus RNA Qualitative Real-Time RT-PCR (Quest Diagnostics Infectious Disease, Inc.)	April 28, 2016 (initial issuance) October 7, 2016 (reissuance) April 11, 2017 (amended)	Authorization (/media/122435/download) (PDF, 339 KB) Letter granting EUA amendment(s) (/media/120127/download) (PDF, 126 KB)	FR notice (https://www.federalregister.gov/articles/2016/06/17/2016-14380/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-zika-virus)
RealStar Zika Virus RT-PCR Kit U.S. (altona Diagnostics GmbH)	May 13, 2016 (initial issuance) October 31, 2016 (amended) March 6, 2017 (amended)	Authorization (/media/120121/download) (PDF, 342 KB) Letter Granting EUA Amendment(s) (/media/120122/download) (PDF, 130 KB) Letter Granting EUA Amendment(s) (/media/120123/download) (PDF, 130 KB)	FR notice (https://www.federalregister.gov/articles/2016/06/17/2016-14380/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-zika-virus)
Aptima Zika Virus assay (Hologic, Inc.)	June 17, 2016 (initial issuance) September 7, 2016 (amended) April 12, 2017 (amended) March 8, 2018 (amended)	Authorization (/media/120114/download) (PDF, 305 KB) Letter granting EUA amendment(s) (/media/122434/download) (PDF, 126 KB) Letter granting EUA amendment(s) (/media/120116/download)(PDF, 124 KB) Letter granting EUA amendment(s) (/media/120117/download)(PDF, 130 KB)	FR notice (https://www.federalregister.gov/articles/2016/07/08/2016-16177/authorizations-of-emergency-use-in-vitro-diagnostic-device-for-detection-of-zika-virus)
Zika Virus Real-time RT-PCR Test (Viracor Eurofins)	July 19, 2016 (initial issuance) February 28, 2017 (amended)	Authorization (/media/120033/download) (PDF, 334 KB) Letter granting EUA amendment(s) (/media/120034/download) (PDF, 124 KB)	FR notice (https://www.federalregister.gov/articles/2016/09/07/2016-21353/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-zika-virus#h-6)
VERSANT Zika RNA 1.0 Assay (kPCR) Kit (Siemens Healthcare Diagnostics Inc.)	July 29, 2016 (initial issuance) December 19, 2016 (amended)	Authorization (/media/99444/download) (PDF, 78 KB) Letter granting EUA amendment(s) (/media/120030/download) (PDF, 124 KB)	FR notice (https://www.federalregister.gov/documents/2016/10/28/2016-26066/emergency-use-authorizations-in-vitro-diagnostic-devices-for-detection-andor-diagnosis-of-zika-virus)
Sentosa SA ZIKV RT-PCR Test (Vela Diagnostics USA, Inc.)	September 23, 2016	Authorization (/media/120017/download) (PDF, 355 KB)	FR notice (https://www.federalregister.gov/documents/2016/11/03/2016-26532/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-zika-virus)

Zika Virus Detection by RT-PCR Test (ARUP Laboratories)	September 28, 2016	Authorization (/media/120014/download) (PDF, 98 KB)	FR notice (https://www.federalregister.gov/documents/2016/11/03/2016-26532/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-zika-virus)
Abbott RealTime ZIKA (Abbott Molecular Inc.)	November 21, 2016 (initial issuance) January 6, 2017 (amended)	Authorization (/media/101657/download) (PDF, 84 KB) Letter granting EUA amendment(s) (/media/120010/download) (PDF, 150 KB)	FR notice (https://www.federalregister.gov/documents/2016/12/20/2016-30532/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-zika-virus)
Zika ELITe MGB Kit U.S. (ELITechGroup Inc. Molecular Diagnostics)	December 9, 2016	Authorization (/media/119919/download) (PDF, 312 KB)	FR notice (https://www.federalregister.gov/documents/2017/01/09/2017-00084/authorization-of-emergency-use-of-an-in-vitro-diagnostic-device-for-detection-of-zika-virus)
Gene-RADAR Zika Virus Test (Nanobiosym Diagnostics, Inc.)	March 20, 2017	Authorization (/media/119915/download) (PDF, 313 KB)	FR notice (https://www.federalregister.gov/documents/2017/06/30/2017-13720/emergency-use-authorizations-in-vitro-diagnostic-devices-for-detection-of-zika-virus)
TaqPath Zika Virus Kit (Thermo Fisher Scientific)	August 2, 2017	Authorization (/media/119906/download) (PDF, 292 KB)	FR notice (https://www.federalregister.gov/documents/2017/10/26/2017-23224/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-zika-virus)
CII-ArboViroPlex rRT-PCR Assay (Columbia University)	August 11, 2017	Authorization (/media/107073/download) (PDF, 377 KB)	FR notice (https://www.federalregister.gov/documents/2017/10/26/2017-23224/authorizations-of-emergency-use-of-in-vitro-diagnostic-devices-for-detection-of-zika-virus)

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Related Links

- Coronavirus Disease 2019 (COVID-19) (/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19)

- Summary of Process for EUA Issuance (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/summary-process-eua-issuance)
- Current Emergency Use Authorizations for Medical Devices (/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations-medical-devices)
- How to Submit a Pre-EUA for *In vitro* Diagnostics (IVDs) to FDA (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/how-submit-pre-eua-in-vitro-diagnostics-fda) (for test manufacturers)
- Information for Laboratories Implementing IVD Tests Under EUA (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/information-laboratories-implementing-ivd-tests-under-eua)
- Process for Publishing Emergency Use Authorizations for Medical Devices During Coronavirus Disease 2019 (https://www.federalregister.gov/documents/2020/06/02/2020-11898/process-for-publishing-emergency-use-authorizations-for-medical-devices-during-coronavirus-disease) (June 2, 2020)
- Emergency Use Authorization--Archived Information (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization-archived-information)
- Emergency Dispensing Orders (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-dispensing-orders)
- 21st Century Cures Act: MCM-Related Cures Provisions (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/21st-century-cures-act-mcm-related-cures-provisions)
- Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/pandemic-and-all-hazards-preparedness-reauthorization-act-2013-pahpra)
- Public Readiness and Emergency Preparedness (PREP) Act (https://www.phe.gov/preparedness/legal/prepact/pages/default.aspx)
- HHS Public Health Emergency EUA Authorization Declarations (http://www.phe.gov/emergency/news/healthactions/Lists/EUA/AllItems.aspx)
- Ebola Preparedness and Response Updates from FDA (/emergency-preparedness-and-response/mcm-issues/ebola-preparedness-and-response-updates-fda)
- Zika Virus Response Updates from FDA (/emergency-preparedness-and-response/mcm-issues/zika-virus-response-updates-fda)
- Historical Information about Device Emergency Use Authorizations (/medical-devices/emergency-situations-medical-devices/historical-information-about-device-emergency-use-authorizations)

Providers: $25.5 billion in Provider Relief Fund & American Rescue Plan rural funding is now available. **Submit your application by October 26, 2021.**

Health Resources & Services Administration

Ensuring Equity in COVID-19 Vaccine Distribution

Engaging Federally Qualified Health Centers

Health Center COVID-19 Vaccine Program is Open to All Health Centers

- View participating and invited health centers
- Frequently Asked Questions
  - Health Center COVID-19 Vaccine Program
  - General COVID-19 vaccination information

To ensure our nation's underserved communities and those disproportionately affected by COVID-19 are equitably vaccinated against COVID-19, the Health Resources and Services Administration (HRSA) and the Centers for Disease Control and Prevention (CDC) launched a program to directly allocate COVID-19 vaccine to HRSA-supported health centers.

During the first phase of the program, HRSA invited 250 health centers to participate. To further expand the program and accelerate the delivery of vaccines to medically underserved communities and disproportionately affected populations, HRSA and CDC invited an additional 700 health centers to participate, increasing the total number of invited health centers to 950. On April 7, 2021, HRSA and CDC invited all HRSA-funded health centers and Health Center Program look-alikes (LALs) to participate in the program, increasing its reach to 1,470 health centers nationwide.

HRSA-funded health centers are community-based and patient-directed organizations that deliver affordable, accessible, quality, and cost-effective primary health care to nearly 30 million patients each year. Over 91% of health center patients are individuals or families living at or below 200% of the Federal Poverty Guidelines and nearly 63% are racial/ethnic minorities. Health centers across the nation are playing vital roles in supporting local community responses to the COVID-19 public health emergency.

Health Center Selections

The initial 250 health centers invited to this program included those that serve a large volume of one of the following disproportionately affected populations:

- Individuals experiencing homelessness,
- Public housing residents,
- Migrant/seasonal agricultural workers, or
- Patients with limited English proficiency

The second group of 700 health centers invited to participate in this program included those that:

- Serve high proportions of low income and minority patients,
- Provide services to rural/frontier populations,
- Operate Tribal/Urban Indian Health Programs, and/or
- Utilize mobile vans to deliver services

The third and final group of 520 health centers included all remaining HRSA-supported health centers, expanding access to COVID-19 vaccinations for underserved communities and vulnerable populations across the country.

Vaccine Supply is in Addition to Jurisdictional Supply

The allocation provided for this program is separate from jurisdictions' weekly allocations. The federal government is providing vaccines to health centers as a way to increase access to vaccines for health centers serving the nation's underserved communities and disproportionately affected populations.

Date Last Reviewed: May 2021

Errata

Vol. 70, No. 27

In the report "Outcomes Among Patients Referred to Outpatient Rehabilitation Clinics After COVID-19 diagnosis — United States, January 2020–March 2021," on page 967, the following authors' names should have read, "Meredith **G. Dixon**, MD" and "Caitlyn **Lutfy**, MPH." On page 970, in Table 3, in the row for "Social participation ability," in the columns for "Post–COVID-19 patients," "Control patients," and "mean difference" the summary scale T-score mean standard deviations and mean differences should have read, "**46.6 (44.7 to 48.6)**," "**50.5 (50.0 to 51.1)**," and " **–4.2 (–6.4 to –2.0)**," respectively.

Vol. 70, No. 30

In the report "Progress Toward Hepatitis B Control — World Health Organization European Region, 2016–2019," on page 1030, in the second column, first paragraph, the last sentence should have read, "Of the 21 countries with universal HepB-BD that reported birth dose coverage to WHO,[†††] coverage with timely HepB-BD during 2016–2019 was ≥90% in **19–20** (90%–95%) **countries**."

BRIEF REPORT

Essential Long-Term Care Workers Commonly Hold Second Jobs and Double- or Triple-Duty Caregiving Roles

Courtney Harold Van Houtven, PhD, MSc,[*†] *Nicole DePasquale, PhD,*[‡] *and Norma B. Coe, PhD*[§]

OBJECTIVES: Long-term care (LTC) facilities are particularly dangerous places for the spread of COVID-19 given that they house vulnerable high-risk populations. Transmission-based precautions to protect residents, employees, and families alike must account for potential risks posed by LTC workers' second jobs and unpaid care work. This observational study describes the prevalence of their (1) second jobs, and (2) unpaid care work for dependent children and/or adult relatives (double- and triple-duty caregiving) overall and by occupational group (registered nurses [RNs], licensed practical nurses [LPNs], or certified nursing assistants [CNAs]).

DESIGN: A descriptive secondary analysis of data collected as part of the final wave of the Work, Family and Health Study.

SETTING: Thirty nursing home facilities located throughout the northeastern United States.

PARTICIPANTS: A subset of 958 essential facility-based LTC workers involved in direct patient care.

MEASUREMENTS: We present information on LTC workers' demographic characteristics, health, features of their LTC occupation, additional paid work, wages, and double- or triple-duty caregiving roles.

RESULTS: Most LTC workers were CNAs, followed by LPNs and RNs. Overall, more than 70% of these workers agreed or strongly agreed with this statement: "When you are sick, you still feel obligated to come into work." One-sixth had a second job, where they worked an average of 20 hours per week, and more than 60% held double- or triple-duty caregiving roles. Additional paid work and unpaid care work characteristics did not significantly differ by occupational group, although the prevalence of second jobs was highest and accompanying work hours were longest among CNAs.

CONCLUSION: LTC workers commonly hold second jobs along with double- and triple-duty caregiving roles. To slow the spread of COVID-19, both the paid and unpaid activities of these employees warrant consideration in the identification of appropriate clinical, policy, and informal supports. **J Am Geriatr Soc 00:1-4, 2020.**

Keywords: long-term care workers; nursing home; second jobs; double- and triple-duty caregiving; COVID-19 pandemic

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Long-term care (LTC) facilities are particularly dangerous places for the spread of COVID-19 as the country first learned with the outbreak in Kirkland, Washington's Life Care Center in early March 2020.[1] This means that the more than 3.6 million people who receive support from an LTC facility in the United States are at heightened risk of infection.[2] As of April 1, 2020, 400 nursing homes nationally reported COVID-19 cases.[3] By April 7, 187 homes reported cases in New Jersey alone,[4] and by April 16, outbreaks had been reported in 3,466 LTC facilities in 39 states,[5] representing more than 5,500 nursing home resident deaths due to COVID-19.[6]

Nursing homes employ more than 940,000 full-time equivalent nursing staff.[7] Before the COVID-19 pandemic, low wages and limited benefits meant that many facility-based LTC workers (hereafter LTC workers) held multiple jobs. As essential workers, they continue to face exposure risks and are part of multiple transmission risk pathways.

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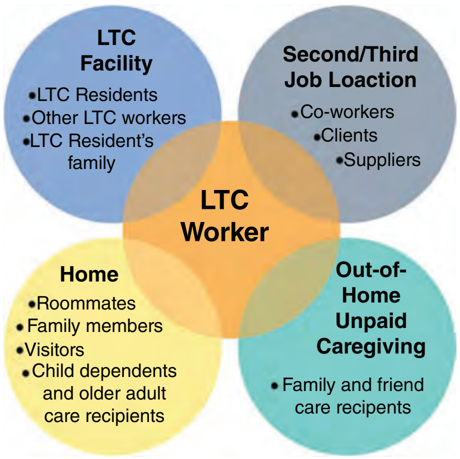

Figure 1 Distinct contact locations of long-term care (LTC) workers.

Not only do we need to consider transmission risk between facility residents to and from LTC workers and between LTC workers to and from their own household members (Figure 1), but additional risks are posed by their second jobs and their unpaid care work in other settings. This article describes the paid and unpaid work of LTC workers to illuminate a potentially potent pathway of COVID-19 transmission risk that should be addressed.

We used data from the final wave of the Work, Family and Health Study (WFHS) to describe the prevalence of (1) second jobs, and (2) unpaid care work for dependent children and/or adult relatives (ie, double- and triple-duty caregiving) among LTC workers.[8] These data are from 2012, but there is little evidence to indicate the situation has changed for LTC worker since then. The LTC sector was essentially left out of healthcare reform (the Affordable Care Act in 2010), and, as such, financing and public reimbursement for nursing homes have not changed.[9] Given

Table 1 Characteristics of Long-Term Care Workers

Characteristics	Overall N = 958	RN n = 101 (10%)	LPN n = 191 (20%)	CNA n = 666 (70%)	*P*
Demographics					
Age, y	40.6 (12.2)	43.7 (12.0)	42.9 (11.8)	39.5 (12.3)	<.001
Female	890 (93%)	95 (94%)	181 (95%)	614 (92%)	.42
White	676 (71%)	77 (76%)	152 (80%)	447 (67%)	<.01
Hispanic	138 (14%)	4 (4%)	8 (4%)	126 (19%)	<.001
Foreign born	275 (29%)	23 (23%)	39 (20%)	213 (32%)	<.01
Married/Living with partner	580 (61%)	77 (76%)	131 (69%)	372 (56%)	<.001
Spouse/Partner has full-time/Part-time job	466 (80%)	67 (87%)	108 (82%)	291 (78%)	.17
Some college or more	595 (62%)	101 (100%)	180 (94%)	314 (47%)	<.001
Total household size	3.1 (1.6)	3.24 (1.8)	3.1 (1.4)	3.1 (1.6)	.70
Health					
At least one chronic condition	342 (36%)	38 (38%)	79 (41%)	225 (34%)	.14
LTC work role					
Hours worked per week at primary job	36.3 (7.6)	37.1 (8.5)	37.1 (6.6)	36.0 (7.6)	.11
Company tenure, y	8.9 (7.1)	8.8 (8.0)	9.6 (7.2)	8.7 (6.9)	.32
Feel obligated to work while sick (agree or strongly agree)	669 (70%)	71 (70%)	135 (71%)	463 (70%)	.38
Additional paid work					
Has second job	167 (17%)	13 (13%)	31 (16%)	123 (19%)	.34
Hours worked per week at second job	19.7 (12.8)	14.7 (15.3)	16.5 (11.4)	21.1 (12.6)	.07
Wages					
Gross annual personal income (range = 1-13)	7.5 (2.9)	11.2 (1.8)	10.5 (2.1)	6.1 (2.0)	<.001
Gross annual household income (range = 1-13)	9.7 (3.2)	12.4 (1.4)	12.1 (1.7)	8.7 (3.1)	<.001
Perceived adequacy of total household income					<.001
We cannot make ends meet	72 (7%)	4 (4%)	12 (6%)	56 (8%)	
We have just enough, no more	294 (31%)	15 (5%)	47 (25%)	232 (35%)	
We have enough, with a little extra sometimes	467 (49%)	67 (66%)	98 (51%)	302 (45%)	
We always have money left over	124 (13%)	15 (15%)	34 (18%)	75 (11%)	
Unpaid care work					
Double-or triple-duty care	582 (61%)	61 (60%)	119 (62%)	402 (61%)	.90

Note: Higher values indicate greater levels of the variable being examined. Chronic conditions included stroke, cancer, high blood pressure, coronary heart disease, and diabetes. Gross annual personal and household income were each measured on a 13-point ordinal scale from 1 = less than $4,999 to 13 = more than $60,000. Double- or triple-duty caregivers lived with at least one child aged 18 years or younger for 4 or more days per week and/or provided unpaid care to at least one adult relative for 3 or more hours per week in the past 6 months regardless of residential proximity.
Abbreviations: CNA, certified nursing assistant; LPN, licensed practical nurse; LTC, long-term care; RN, registered nurse.

that labor is the biggest share of the costs of nursing home operations and Medicaid reimbursement rates remain low, LTC worker wages have increased on average 1% in real terms over the past 10 years.[10] In tandem, beyond possibly gaining their own health insurance coverage through healthcare reform, there is no evidence that LTC worker conditions have changed in the past decade. The workforce remains predominantly female and is ethnically and racially diverse. Injuries remain high compared with other occupations,[11] wages remain extremely low, and fringe benefits are minimal.[12] Therefore, this unique data source from 2012 can illuminate behaviors of today's LTC workforce.

METHODS

The WFHS was designed to examine the work, family, and health of employees working in 30 nursing home facilities throughout New England.[13] The most recent and final wave of data collection was completed in December 2012 (N = 1,007). We focused on the subset of study participants providing direct patient care including registered nurses (RNs), licensed practical nurses (LPNs), and certified nursing assistants (CNAs) (n = 958). We present descriptive data on secondary jobs and double- or triple-duty caregiving roles by all LTC workers and by occupational groups. Specifically, we estimate means and standard deviations for continuous variables and for distributions and frequencies for categorical variables. The *P* values for differences among the three occupational groups were obtained from the analysis of variance method for continuous variables and χ^2 tests for categorical variables. Duke University deemed this study as exempt (00105391).

RESULTS

Overall, the mean age of LTC workers was 41 years (Table 1). Most LTC workers were female, white, married or living with a partner, and had some college or more education. A minority were Hispanic and foreign born, and more than one-third reported a chronic condition. The average total household size was three. Of those with a spouse or partner, 80% were dual-earner couples. The LTC work role was a full-time position held on average for nearly 10 years. More than 70% agreed or strongly agreed with this statement: "When you are sick, you still feel obligated to come into work."[14] One-sixth of LTC workers had a second job, where they worked an average of 20 hours per week. The mean annual gross personal and household income brackets were $30,000 to $34,999 and $40,000 to $44,999, respectively. When asked which of four statements best described their ability to get along on their household income,[15] most (51%) LTC workers chose, "We have enough, with a little extra sometimes." Most LTC workers held double- or triple-duty caregiving roles (61%).

Among the three occupational groups, CNAs significantly differed from RNs and LPNs on several demographic characteristics. CNAs were younger, more often Hispanic, less often married or living with a partner, and proportionately fewer had obtained some college or more education. Additionally, a significantly lower proportion of CNAs were white and US born compared with LPNs. CNAs also significantly differed from their counterparts with respect to wages. CNAs reported lower gross annual personal and household incomes than both RNs and LPNs. Further, LPNs had a lower gross annual personal income relative to RNs. Perceived adequacy of household income significantly differed by occupational group; RNs more frequently endorsed the statement "We have enough, with a little extra sometimes" (66%) compared with both LPNs (51%) and CNAs (45%). All occupational groups were similar in characteristics pertaining to health, the LTC work role, additional paid work, and unpaid work. Descriptively, the prevalence of second jobs was highest and accompanying work hours were longest among CNAs. At least 60% of LTC workers across all occupations held double- or triple-duty caregiving roles.

DISCUSSION

This analysis is descriptive and provides no causal explanation behind holding second jobs and multiple caregiving roles. In addition to these data dated from 2012, the WFHS represents LTC workers from one region of the United States. And yet we are encouraged that the wages, sex, and foreign-born profiles in the WFHS mirror those seen in LTC workers nationally.[16] Given its regional focus, the WFHS workers may not represent the countries of origin of workers in other regions. Overall, however, this is a unique data set with high relevance to the COVID-19 pandemic today, and the findings lead us to several immediate policy recommendations.

To minimize spread of COVID-19, we need to consider the lives of LTC workers such as those described here. First, the high proportion holding a second job means that risk of spread is higher to and from multiple locations (eg, Figure 1). Their own preexisting health conditions make many LTC workers high risk on their own. They commonly also live with other household members, so their own risks could endanger their own families. A high percentage of their partners are working, and depending on their careers, they may or may not be able to shelter at home.

Facilities could institute policies to help mitigate disease transmission risk. Changing the culture to decrease the obligation to work when sick would be a start. Also called presenteeism, being at work when sick puts everyone at risk: colleagues, residents, and visitors alike. Providing sick leave and benefits would reduce this obligation. These benefits could especially help the lowest wage workers such as CNAs, who are most likely to work a second job. Similarly, increasing wages so that workers can work just one job could mitigate risk to the LTC worker, the LTC residents, and to families by limiting the potential for cross-contamination. To protect their residents from COVID-19, high-end independent living facilities are instituting a rule whereby shifts are only given to workers who do not have a second job. However, without wage or hour increases, this policy will financially penalize the 17% of LTC workers who also work part time elsewhere.

States and the federal government could also mitigate disease transmission risk. Immediately increasing Medicaid and Medicare reimbursement rates during the COVID-19 pandemic could allow firms to increase pay to their direct care workers. These firms do not have high profit margins, and they are also likely to be suffering economic losses due

to fewer non–COVID-19 post-acute care patients during the pandemic; increasing wages is unlikely to be a unilateral move from private firms. Framing increased reimbursement as supporting extending hazard pay to workers could frame the move as temporary to meet the needs of the COVID-19 pandemic.

Finally, informal support for LTC workers, especially those who are double- or triple-duty caregivers, is urgently needed if they are to remain healthy and continue to be effective in their vital roles in and beyond the LTC setting. A temporary shift of unpaid care work to capable nonessential employees or other members of LTC workers' social networks, for example, may help these essential workers self-isolate and decrease opportunities for transmission. Undoubtedly, a shift in primary responsibility for unpaid care to secondary or new family caregivers throws many into unchartered territory; such changes to decrease transmission risk could be facilitated through extending state and federal resources and guidance for caregiving to families.

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Clinical Infectious Diseases
MAJOR ARTICLE

Estimated Incidence of Coronavirus Disease 2019 (COVID-19) Illness and Hospitalization—United States, February–September 2020

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(See the Major Article by Basavaraju et al on pages e1004–9 and the Editorial Commentary by Rosenberg and Bradley on pages e1018–20).

Background. In the United States, laboratory-confirmed coronavirus disease 2019 (COVID-19) is nationally notifiable. However, reported case counts are recognized to be less than the true number of cases because detection and reporting are incomplete and can vary by disease severity, geography, and over time.

Methods. To estimate the cumulative incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, symptomatic illnesses, and hospitalizations, we adapted a simple probabilistic multiplier model. Laboratory-confirmed case counts that were reported nationally were adjusted for sources of underdetection based on testing practices in inpatient and outpatient settings and assay sensitivity.

Results. We estimated that through the end of September, 1 of every 2.5 (95% uncertainty interval [UI]: 2.0–3.1) hospitalized infections and 1 of every 7.1 (95% UI: 5.8–9.0) nonhospitalized illnesses may have been nationally reported. Applying these multipliers to reported SARS-CoV-2 cases along with data on the prevalence of asymptomatic infection from published systematic reviews, we estimate that 2.4 million hospitalizations, 44.8 million symptomatic illnesses, and 52.9 million total infections may have occurred in the US population from 27 February–30 September 2020.

Conclusions. These preliminary estimates help demonstrate the societal and healthcare burdens of the COVID-19 pandemic and can help inform resource allocation and mitigation planning.

Keywords. COVID-19; disease burden; pandemic.

In the United States, the earliest known patients with coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, were associated with travel to affected countries or known contact with other infected persons [1]. By February 2020, persons with SARS-CoV-2 infection in the United States and no known exposure were detected [2]. Between 27 February and 30 September 2020, nearly 6.9 million laboratory-confirmed cases of domestically acquired infections were detected and reported nationally.

Persons with laboratory-confirmed SARS-CoV-2 infection reported through national surveillance do not represent all infected persons in the United States. Seroprevalence studies have shown a higher level of SARS-CoV-2 infection than has been reflected by confirmed case counts [3–7]. Most unreported infections were asymptomatic or mildly ill people who recovered without seeking medical care or testing [8–10]. However, even persons with SARS-CoV-2 infection in medical settings may not be tested or nationally reported as confirmed cases. Limited availability of tests, reagents, and laboratory capacity reduced case detection; in addition, patients may have avoided medical care settings or presented with nonspecific symptoms and not been suspected to have SARS-CoV-2 infection. Furthermore, not all infected persons will test positive because of assay sensitivity, timing of specimen collection, or specimen quality [11]. Factors involved in detecting and reporting cases may vary by age, geographically, over time, across healthcare settings, and by severity of disease. Finally, some people may be infected with SARS-CoV-2 and never show clinical symptoms; these asymptomatic persons would be even less likely to be detected [9, 10].

To better estimate the US incidence of SARS-CoV-2 infection since the beginning of the pandemic, we adapted a probabilistic multiplier model to adjust nationally reported counts of confirmed cases for various sources of underdetection [12]; this model estimates total SARS-CoV-2 infections, symptomatic illnesses, and hospitalized patients in the US population from 27 February 2020 to 30 September 2020.

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METHODS

Reported Confirmed Cases

Persons with laboratory-confirmed SARS-CoV-2 infection by molecular diagnostics are reported to the Centers for Disease Control and Prevention (CDC) through the Nationally Notifiable Disease Surveillance System (NNDSS) at the person level or as aggregate counts at the reporting jurisdiction level (eg, state, territory, New York City, District of Columbia) [13, 14]. The NNDSS uses a standardized case report form, including state of residence, age, hospitalization admission, and other demographic and clinical characteristics. Given data entry delays and incomplete national reporting, jurisdictions reported aggregated counts daily for the previous day. Probable, asymptomatic, and travel-associated cases were excluded from counts of confirmed cases used in this analysis.

Analytic Methods

We applied a probabilistic multiplier model to adjust the reported numbers of confirmed symptomatic cases for factors affecting detection of persons with SARS-CoV-2 infection, a method previously used to estimate the incidence of H1N1pdm09 during the 2009 influenza pandemic [12]. This method uses confirmed cases and data on case detection and the asymptomatic fraction to estimate the cumulative number of hospitalized patients with SARS-CoV-2 infection, the total number with symptomatic illness, and the total number of infected persons (Figure 1).

To account for variability in detection of SARS-CoV-2 we stratified reported cases into hospitalized and nonhospitalized symptomatic cases, and further by age group (0–4 years, 5–17 years, 18–49 years, 50–64 years, ≥65 years), time period when the case was reported (February–March, April–May, June–July, August–September), and US Department of Health and Human Services (HHS) region [15]. Age group was imputed for cases with missing birth date according to the age distribution within each HHS region and reporting time period. If hospitalization status was missing, we imputed the percentage of patients who were hospitalized based on reported cases with complete data by age group, HHS region, and reporting time period. More details on this process are available in the Supplementary Methods.

We adjusted case counts for 3 factors that affected national case detection of symptomatic cases: if a patient is symptomatic, they may not have sought medical attention or testing for their illness (parameter C); if a patient sought medical care, they may not have had a SARS-CoV-2 test completed (parameter B); or if a patient was tested, the SARS-CoV-2 assay used may result in a false-negative result due to its sensitivity to detect SARS-CoV-2 in the specimen (parameter A). We used several data sources to describe these factors (Table 1), with underdetection multipliers calculated as an inverse of the product of factors A–C. Each multiplier was calculated within strata of hospitalization status, age group, and reporting time period, as data were available, and applied to the relevant stratified cases counts to estimate the number of symptomatic cases within that strata.

After adjustment, we summed the strata to a number of estimated symptomatic cases and applied one more source of underdetection—a person infected with SARS-CoV-2 may never show clinical symptoms (parameter D)—to estimate the number of total infections in the population.

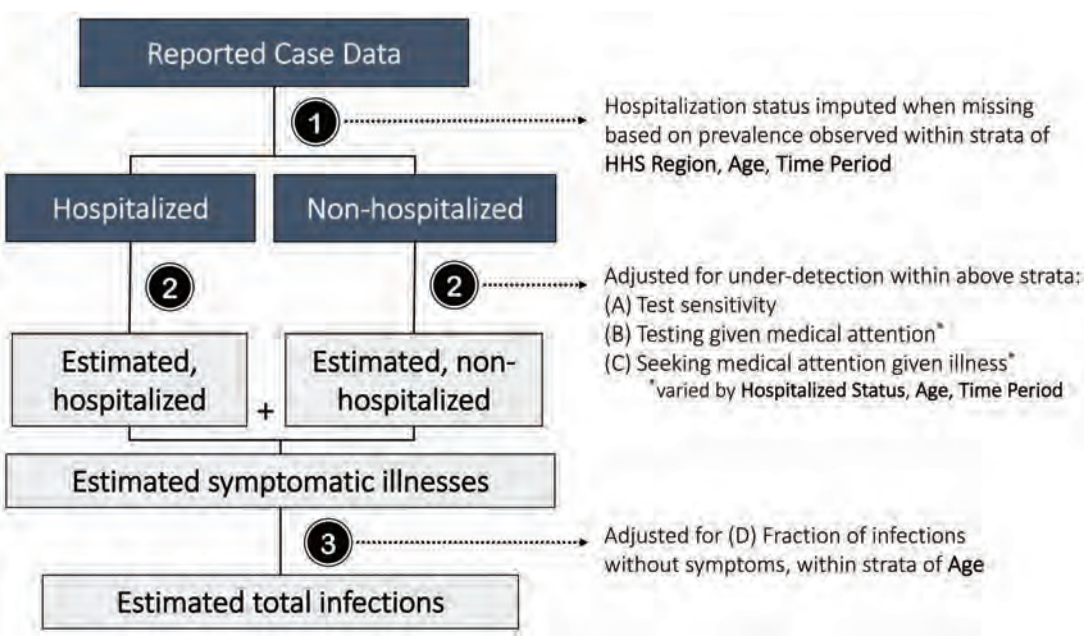

Figure 1. Flow diagram of the methods to estimate total numbers of hospitalized, symptomatic illnesses, and infections from SARS-CoV-2 in the United States through adjustment of nationally reported case counts. Abbreviations: HHS, Department of Health and Human Services; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1. Sources of Underdetection Included in Model-Based Estimates of the Incidence of COVID-19: United States, February–September 2020

	Parameter	Data Source [reference]	Observed Value	Statistical Distribution Included in Model
Hospitalized				
A	SARS-CoV-2 assay sensitivity	Systematic review [16]	2%–21% False-negative rate across included studies	Uniform (0.79, 0.98) (same values as non-hospitalized)
B	SARS-CoV-2 test ordered and completed	IBM Watson and COVID Near You	Median (range): 0–17 years, 33% (15%–55%); 18–49 years, 50% (21%–96%); 50–64 years, 51% (18%–97%); ≥65 years, 54% (6%–98%)	Beta PERT, varies by age and date of case report (see Supplementary Table 1) (values specific to hospitalized settings)
Nonhospitalized				
A	SARS-CoV-2 assay sensitivity	Systematic review [16]	2%–21% False-negative rate across included studies	Uniform (0.79, 0.98) (same values as hospitalized)
B	SARS-CoV-2 test ordered and completed	IBM Watson and COVID Near You	Median (range): 0–17 years, 43% (1%–71%); 18–49 years, 53% (6%–99%); 50–64 years, 58% (6%–98%); ≥65 years, 54% (6%–99%)	Beta PERT, varies by age and date of case report (see Supplementary Table 1) (values specific to outpatient settings)
C	Symptomatic patient seeks care	COVID Near You and Flu Near You	Median (range): 0–17 years, 26% (13%–49%); 18–49 years, 34% (15%–65%); 50–64 years, 35% (13%–55%); ≥65 years, 40% (11%–60%)	Beta PERT, varies by age and HHS region (see Supplementary Table 2) (values specific to outpatient settings)
Total infections				
D	Infected person is asymptomatic	[8, 17]	0–64 years: 5%–24%; ≥65 years: 5%–32%	Uniform, varies by age

Abbreviations: COVID-19, coronavirus disease 2019; HHS, Department of Health and Human Services; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

For all parameters and strata, we included a range of values; estimates were calculated using Latin hypercube sampling with 10 000 iterations, with 95% uncertainty intervals (UIs) estimated as the 2.5th and 97.5th percentile range. Population rates were estimated using bridged-race population estimates from CDC Wonder [18]. Analyses were completed in R (version 3.6.1; R Foundation for Statistical Computing).

Sources of Underdetection of Cases

Parameter A. SARS-CoV-2 Assay Sensitivity

Patients infected with SARS-CoV-2 may not always test positive. Sensitivity of approved molecular diagnostic assays may be affected by the limits of detection of specific assays, specimen quality, source, handling, and timing of collection [11]. In a systematic review, 2%–21% of patients ultimately confirmed to have SARS-CoV-2 infection did not have a positive result unless multiple tests were performed over several days [16]. This review was used to estimate the probability that a specimen with SARS-CoV-2 will test positive (Table 1). For simplicity, since reported assay specificity has been high with false-positive results ranging between 1% and 4% [19, 20], we did not adjust for potential false positives.

Parameter B. SARS-CoV-2 Assay Ordered and Test Completed

Patients with SARS-CoV-2 infection who are not tested with molecular assays are not included in confirmed case counts. To characterize testing probabilities, we used data from 2 sources on healthcare visits and SARS-CoV-2 testing, and estimated this parameter separately for hospitalized and nonhospitalized patients. To capture the variability in testing practices across data sources, we represented this parameter using a beta PERT distribution centered on the median value and ranging between the minimum and maximum values reported across both data sources within each stratum of age (Table 1). The beta PERT distribution is a continuous probability distribution, which emphasizes the most likely values in an acceptable range of parameter values (ie, more often drawing closer to the middle value of the interval with a smaller probability on the extremes of the interval).

The first source of data was the IBM Watson Health Explorys electronic health record (EHR) database (IBM Corporation, Armonk, NY), which includes more than 39 health system partners across the country. We identified visits with an International Classification of Diseases, 10th revision (ICD-10), diagnosis or Systematized Nomenclature of Medicine Clinical Terms (SNOMED) code that indicated an acute respiratory illness (ARI) (Supplementary Table 7) and the number of those with evidence of SARS-CoV-2 test results from Logical Observation Identifiers Names and Codes (LOINC) codes for SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) tests (Supplementary Table 8). For each setting (inpatient, outpatient, emergency department), visits and tests performed were aggregated into strata for time period and age group.

We also included rates of testing in the COVID Near You (CNY) survey platform. CNY is a website application where participants can self-report symptoms, healthcare-seeking behaviors, and SARS-CoV-2 testing information [21–23]. COVID-like illness (CLI) was defined using self-reported presence of shortness of breath or cough or 2 or more of self-reported fever, chills, sore throat, body ache, headache, or loss of taste or smell. Proportions of individuals who self-reported receiving a SARS-CoV-2 test among those who sought care for CLI were estimated for each time period with available data by HHS region and age group (Table 1, Supplementary Table 1).

Parameter C. Symptomatic Patient Seeks Care/Testing

A symptomatic person with SARS-CoV-2 infection will not be included in confirmed case counts if they never sought medical

attention or testing services. To estimate healthcare seeking, we used data obtained from both CNY and Flu Near You (FNY) [24], which has conducted participatory surveillance for influenza-like illnesses since 2011, to better capture the full time period and differences between participants of the 2 systems. We considered a range of symptomatic illness including the following: (1) CLI as described above, but excluding loss of taste or smell for FNY, which was not captured in that platform; (2) a more specific case definition of fever, and either cough or shortness of breath; and (3) a broader case definition of at least 1 of fever, cough, or shortness of breath. Among patients who met the given case definition, we calculated the proportion who reported visiting a doctor's office, urgent care clinic, outpatient clinic, emergency department, testing center, telemedicine, or other healthcare setting for symptoms. Care-seeking proportions were included using a beta PERT distribution of the median and range of values across the 3 case definitions and 2 data sources, stratified by report date and age group (Table 1, Supplementary Table 2).

Parameter D. Patient Is Symptomatic if Infected With SARS-CoV-2

Some people infected with SARS-CoV-2 do not experience symptoms [25]. To estimate the number of infections in the population, we adjusted the sum of hospitalized and symptomatic nonhospitalized cases based on the proportion of persons with confirmed COVID-19 and no symptoms from a meta-analysis of available literature (Table 1) [17].

RESULTS

National Case Reporting

During 27 February–30 September 2020, there were 6 891 764 confirmed cases of symptomatic COVID-19 acquired domestically and reported nationally through individual or aggregate case counts. We estimated that approximately 14% of these patients had been hospitalized, with variation by age group, case report date, and HHS region (Table 2).

Hospitalized Cases

We estimated 2.5 (95% UI: 2.0–3.1) SARS-CoV-2 hospitalizations in the population for each hospitalized case reported nationally, with variations by age group, HHS region, and report date. Underdetection multipliers decreased over time and were consistently highest among children (Supplementary Table 3).

Adjusting case counts by HHS region, age group, and report date, we estimated a total of 2 397 777 (95% UI: 2 053 156–2 855 843) hospitalizations with SARS-CoV-2 infection (Table 3), or 733 hospitalizations per 100 000 population. The highest rates of hospitalization were among patients aged 65 years and older (1950/100 000) and lowest among children 5–17 years of age (83/100 000). Estimates varied geographically: 236 per 100 000 in HHS region 10 to 2440 per 100 000 in HHS region 2.

Nonhospitalized Symptomatic Illnesses

We estimated 7.1 (95% UI: 5.8–9.0) nonhospitalized symptomatic illnesses for every 1 nonhospitalized case reported

Table 2. Reported Laboratory-Confirmed COVID-19 Cases and Hospitalization Status, by Age and Region: United States, February–September 2020

	Reported Cases, n	Rate of Reported Cases, per 100 000 Population[a]	Percentage of Reported Cases Hospitalized, Median[b,c]	Rate of Reported Hospitalization, Median, per 100 000 Population[a,b]
Total	6 891 764	2106	14	296
Age group (years)				
0–4	109 317	552	6	31
5–17	458 552	856	3	26
18–49	3 974 817	2877	7	195
50–64	1 377 416	2181	19	418
≥65	971 662	1853	43	789
HHS region				
1 (CT, MA, ME, NH, RI, VT)	208 808	1406	19	271
2 (NJ, NY, PR, VI)[c]	679 581	2389	33	786
3 (DE, DC, MD, PA, VA, WV)	468 065	1518	14	208
4 (AL, FL, GA, KY, MS, NC, SC, TN)	1 769 052	2664	9	241
5 (IL, IN, MI, MN, OH, WI)	882 355	1679	15	258
6 (AR, LA, NM, OK, TX)	1 092 515	2576	12	312
7 (IA, KS, MO, NE)	308 636	2185	8	174
8 (CO, MT, ND, SD, UT, WY)	200 390	1651	7	123
9 (AZ, CA, HI, NV, AS, MP, FSM, GU, RMI, PW)	1 117 180	2183	14	310
10 (AK, ID, OR, WA)	165 182	1162	8	92

Patient age was imputed if missing (17% of cases).

Abbreviations: AS, American Samoa; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; FSM, Federated States of Micronesia; GU, Guam; HHS, Department of Health and Human Services; MP, Northern Mariana Islands; NYC, New York City; PR, Puerto Rico PW, Palau; RMI, Marshall Islands; VI, US Virgin Islands.

[a]Population estimated using CDC Wonder Bridged-Race estimates [18].

[b]Patient hospitalization status imputed if missing (86% of cases).

[c]For hospitalization imputation, the regional proportion of cases reported as hospitalized in region 2 was estimated excluding NYC due to a large discrepancy between national and jurisdiction reports.

Table 3. Estimates of Hospitalized Persons with COVID-19 and Rates per 100 000 Population: United States, February–September 2020

	Estimated Hospitalizations	95% UI	Rate, per 100 000[a]	95% UI
Overall[b]	2 397 777	2 053 156–2 855 843	733	628–873
Age group (years)				
0–4	20 719	16 595–26 069	105	84–132
5–17	44 321	33 300–58 552	83	62–109
18–49	652 741	530 955–823 453	472	384–596
50–64	642 358	538 092–778 266	1017	852–1232
≥65	1 022 295	826 438–1 361 730	1950	1576–2597
HHS region				
1 (CT, MA, ME, NH, RI, VT)	103 347	86 983–125 978	696	586–848
2 (NJ, NY, PR, VI)[c]	694 079	580 828–878 399	2440	2042–3087
3 (DE, DC, MD, PA, VA, WV)	152 597	129 196–181 597	495	419–589
4 (AL, FL, GA, KY, MS, NC, SC, TN)	349 780	289 336–423 126	527	436–637
5 (IL, IN, MI, MN, OH, WI)	330 948	278 985–395 956	630	531–754
6 (AR, LA, NM, OK, TX)	288 441	231 390–357 417	680	546–843
7 (IA, KS, MO, NE)	55 692	45 600–68 225	394	323–483
8 (CO, MT, ND, SD, UT, WY)	39 413	33 449–47 559	325	276–392
9 (AZ, CA, HI, NV, AS, MP, FSM, GU, RMI, PW)	347 069	291 807–414 925	678	570–811
10 (AK, ID, OR, WA)	33 552	28 430–41 594	236	200–293

Abbreviations: AS, American Samoa; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; FSM, Federated States of Micronesia; GU, Guam; HHS, Department of Health and Human Services; MP, Northern Mariana Islands; NYC, New York City; PR, Puerto Rico; PW, Palau; RMI, Marshall Islands UI, uncertainty interval.

[a]Population estimated using CDC Wonder Bridged-Race estimates [18].

[b]Due to rounding, age group and region estimates may not sum to overall estimates.

[c]For hospitalization imputation, the regional proportion of cases reported as hospitalized in region 2 was estimated excluding NYC due to a large discrepancy between national and jurisdiction reports.

nationally, with variation by age group, HHS region, and report date. Underdetection multipliers decreased over time and were consistently highest among children (Supplementary Table 3).

We summed the estimated hospitalized (Table 3) and nonhospitalized (Supplementary Table 5) illnesses for a total of 44.8 million symptomatic illnesses (Table 4). The highest rates of symptomatic illness were among adults 18–49 years old (18 162/100 000) and were lowest among children aged 0–4 years (5777/100 000). Estimates varied geographically: 8282 per 100 000 in HHS region 10 to 26 705 per 100 000 in HHS region 2.

Table 4. Estimates of Symptomatic Illnesses From SARS-CoV-2 Infection and Rates per 100 000 Population: United States, February–September 2020

	Estimated Symptomatic Illnesses	95% UI	Rate, per 100 000[a]	95% UI
Overall[b]	44 769 417	36 920 353–55 535 659	13 684	11 285–16 975
Age group (years)				
0–4	1 144 532	903 194–1 500 315	5777	4559–7573
5–17	4 719 785	3 722 649–6 177 733	8807	6947–11 528
18–49	25 096 725	19 137 381–34 524 124	18 162	13 850–24 985
50–64	8 926 318	6 873 250–11 928 318	14 133	10 883–18 887
≥65	4 556 384	3 569 223–6 172 269	8690	6807–11 772
HHS region				
1 (CT, MA, ME, NH, RI, VT)	1 613 724	1 321 058–2 018 578	10 864	8894–13 590
2 (NJ, NY, PR, VI)	7 597 800	5 828 412–10 470 229	26 705	20 486–36 801
3 (DE, DC, MD, PA, VA, WV)	3 179 080	2 627 466–3 915 693	10 307	8519–12 696
4 (AL, FL, GA, KY, MS, NC, SC, TN)	10 263 209	8 428 418–12 805 689	15 457	12 694–19 286
5 (IL, IN, MI, MN, OH, WI)	5 351 673	4 327 360–6 904 494	10 185	8236–13 141
6 (AR, LA, NM, OK, TX)	6 200 307	5 074 596–7 815 354	14 618	11 964–18 426
7 (IA, KS, MO, NE)	1 796 811	1 456 136–2 307 574	12 722	10 310–16 339
8 (CO, MT, ND, SD, UT, WY)	1 329 434	1 087 300–1 676 711	10 952	8957–13 813
9 (AZ, CA, HI, NV, AS, MP, FSM, GU, RMI, PW)	6 155 322	5 093 684–7 539 673	12 026	9952–14 731
10 (AK, ID, OR, WA)	1 177 495	956 766–1 476 146	8282	6729–10 382

Abbreviations: AS, American Samoa; CDC, Centers for Disease Control and Prevention; FSM, Federated States of Micronesia; GU, Guam; HHS, Department of Health and Human Services; MP, Northern Mariana Islands; PR, Puerto Rico; PW, Palau; RMI, Marshall Islands; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; UI, uncertainty interval; VI, US Virgin Islands.

[a]Population estimated using CDC Wonder Bridged-Race estimates [18].

[b]Due to rounding, age group and region estimates may not sum to overall estimates.

Total Infections

Using age-stratified estimates of the proportion of infections that remain asymptomatic, we estimated that the nationally reported cases during February–September may represent a total of 52 885 526 (95% UI: 42 527 569–66 810 205) SARS-CoV-2 infections in the US population, with the highest infection rates among persons aged 18–49 years (Table 5). This indicates that 1 in 7.7, or 13%, of total infections were identified and reported. Detection varied by age, with lower detection rates among children, but with improvements over time (Supplementary Table 4).

DISCUSSION

We estimated that nearly 53 million SARS-CoV-2 infections, including 45 million symptomatic illnesses and 2.4 million associated hospitalizations, may have occurred in the United States through 30 September 2020, with variation by geographic region, age group, and time. These preliminary estimates demonstrate the large incidence of disease in the US population and better quantify the impact of the COVID-19 pandemic on the healthcare system and society, and will be updated as more data on underdetection become available.

From past experiences with influenza [26], another respiratory virus associated with a large proportion of mild illness and an overlapping clinical syndrome with COVID-19, laboratory-confirmed cases reported through surveillance systems underestimate total infections. We adapted our current approach from methods to estimate the influenza A/H1N1pdm09 prevalence in the United States during the 2009 pandemic [12]. Our preliminary estimates indicate approximately 1 in 8, or 13%, of total SARS-CoV-2 infections were recognized and reported through the end of September. Similarly, a recent serologic survey of SARS-CoV-2 antibodies in 10 geographically diverse US sites from 23 March to 12 May of 2020 estimated that the total number of SARS-CoV-2 infections was at least 10 (range by US site: 6–24) for every reported case [3], with improvements in this ratio by later time points. Severe cases were more likely to be detected and reported; we estimated 2.5 hospitalized patients for each hospitalized case reported. In the Explorys EHR data, the proportion of intensive care unit patients tested for SARS-CoV-2 was more than 90% by the end of September, although testing remained lower among other inpatients with ARI, and even lower for ARI visits in outpatient settings (Supplementary Figure 1, Supplementary Table 6).

For comparison, the COVID-19–associated Hospitalization Surveillance Network (COVID-NET) is an active, population-based surveillance system for laboratory-confirmed SARS-CoV-2–associated hospitalizations in defined areas of 14 states [27]. While direct comparisons with COVID-NET are imperfect due to the narrower geographic area of the surveillance sites, in 10 of the 14 sites our estimated hospitalization rates by region were 1.5–3.5 times higher than the reported rates from individual sites within those regions by the end of September, similar to the range of our estimated underdetection multiplier for confirmed hospitalizations. Likewise, COVID-NET showed similar trends across age; adults aged 65 years and older had 5–6 times higher rates of hospitalizations than younger adults aged 18–49 years [28]. Both also showed lower hospitalization rates among children [29, 30].

Table 5. Estimates of Total Infections and Rates Per 100 000 Population: United States, February–September 2020

	Estimated Total Infections	95% UI	Rate, per 100 000[a]	95% UI
Overall[b]	52 885 526	42 527 569–66 810 205	16 165	12 999–20 421
Age group (years)				
0–4	1 342 212	1 022 465–1 811 583	6775	5161–9145
5–17	5 538 766	4 222 053–7 451 900	10 336	7879–13 906
18–49	29 421 481	21 798 393–41 330 693	21 292	15 775–29 911
50–64	10 484 802	7 860 849–14 346 364	16 601	12 446–22 715
≥65	5 636 607	4 139 528–8 024 420	10 750	7895–15 305
HHS region				
1 (CT, MA, ME, NH, RI, VT)	1 910 156	1 530 556–2 427 485	12 860	10 304–16 343
2 (NJ, NY, PR, VI)	8 977 706	6 780 805–12 534 610	31 555	23 834–44 057
3 (DE, DC, MD, PA, VA, WV)	3 759 656	3 025 633–4 721 730	12 190	9810–15 309
4 (AL, FL, GA, KY, MS, NC, SC, TN)	12 107 021	9 741 202–15 448 374	18 234	14 671–23 266
5 (IL, IN, MI, MN, OH, WI)	6 324 790	5 002 112–8 272 471	12 037	9520–15 744
6 (AR, LA, NM, OK, TX)	7 315 403	5 856 636–9 423 602	17 248	13 808–22 218
7 (IA, KS, MO, NE)	2 122 340	1 684 158–2 788 524	15 027	11 925–19 744
8 (CO, MT, ND, SD, UT, WY)	1 569 175	1 250 443–2 013 970	12 927	10 301–16 591
9 (AZ, CA, HI, NV, AS, MP, FSM, GU, RMI, PW)	7 243 925	5 876 211–9 098 261	14 153	11 481–17 776
10 (AK, ID, OR, WA)	1 391 488	1 106 862–1 775 644	9787	7785–12 489

Abbreviations: AS, American Samoa; CDC, Centers for Disease Control and Prevention; FSM, Federated States of Micronesia; GU, Guam; HHS, Department of Health and Human Services; MP, Northern Mariana Islands; PR, Puerto Rico; PW, Palau; RMI, Marshall Islands; UI, uncertainty interval; VI, US Virgin Islands.

[a]Population estimated using CDC Wonder Bridged-Race estimates [18].

[b]Due to rounding, age group and region estimates may not sum to overall estimates.

For comparison of population-level incidence of infection, the estimated 36 million infections represent approximately 16% of the US population, ranging from 9% to 31% across regions of the country. This is higher than seroprevalence estimates from a nationwide commercial laboratory seroprevalence survey, which found that 1%–22% of various state populations had antibodies to SARS-CoV-2 by early August, although our estimates include 2 more months of circulation [31]. There remain uncertainties in the interpretation of seroprevalence estimates, including how they vary by the population surveyed, the serologic assays used, the proportion of infected cases with a detectable antibody response, and how long antibody detection persists after infection. Additional studies and sources of data on population-based incidence will help resolve these concerns and provide better national estimates of illness and infection.

We recognize that our model has limitations. From almost a decade of monitoring data on testing practices for influenza [32, 33], testing rates and the use of more sensitive molecular testing have varied by jurisdictions, care settings, age, and disease severity [34]. The availability and use of testing for SARS-CoV-2 have changed rapidly over time; thus far, data on the proportion of persons who are tested for COVID-19 and how this varies across all the previously described factors remain limited. Although data on testing by time, healthcare setting, and age were available, they lacked the coverage to allow for geographic-specific model inputs. These data limitations could have resulted in overestimation of cases from areas with higher testing rates, including some hospitals that are performing universal testing or have more outpatient testing facilities and active contact tracing. Likewise, we may have underestimated in areas with lower testing and contact tracing. Additionally, some infections, such as those among healthcare workers or from outbreaks in congregate residential settings, may be more likely to be tested and nationally reported compared with the general population, and could overestimate nonhospitalized cases and infections. We continue to seek information on the proportion of cases and testing rates in various settings to improve estimates. With limited but growing information regarding the spectrum of clinical manifestations from SARS-CoV-2 infection, there could be a lower index of suspicion of COVID-19 for patients who present with nonspecific and nonrespiratory symptoms; these cases may be less likely to be detected and reported. All of this highlights the importance of having data to monitor the proportions of patients with different clinical syndromes who are being tested for SARS-CoV-2 infection in a variety of healthcare and geographic settings, and not just total numbers of tests performed. Finally, in some heavily affected areas, the size of the outbreaks exceeded capacities to complete detailed case reporting, including patient age and hospitalization status. For cases with missing hospitalization status, we imputed the proportion of reported cases who were hospitalized from the subset with complete data, but it is unclear if age and hospitalization status were missing at random [35]. If not random, and the data were more complete for hospitalized patients, the true hospitalization rate would be lower than we imputed, and the number of hospitalized cases would be lower than we estimated. Furthermore, this was hospitalization status at the time of the case report and would miss those diagnosed as an outpatient but who became hospitalized after they were reported as a case; thus, our estimates of hospitalization may be an underestimate.

Despite these limitations, our model provides a relatively simple approach to illustrate why there are more persons who have had a SARS-CoV-2 infection than the reported confirmed case counts at multiple levels of disease severity. We used data currently available to provide a preliminary estimate of the overall incidence of SARS-CoV-2 infection, illness, and hospitalization in the United States. The CDC is actively working on refining methods to synthesize information across multiple data sources to better describe the national burden of SARS-CoV-2 infection on an ongoing basis and will update estimates as data become available.

In summary, we estimated that in the United States through 30 September 2020 there were approximately 53 million total SARS-CoV-2 infections, including 45 million symptomatic illnesses and 2.4 million hospitalizations, with large variations by age group and geographic area. This indicates that approximately 84% of the US population has not yet been infected and thus most of the country remains at risk, despite already high rates of hospitalization. Improved estimates of SARS-CoV-2 infections, symptomatic illnesses, and hospitalizations over time are critical to our understanding of the severity and burden of this new virus.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Estimating real-world COVID-19 vaccine effectiveness in Israel using aggregated counts

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Abstract

The vaccination roll-out of the COVID-19 vaccines in Israel has been highly successful. By February 22th, approximately 47% of the population has already been administered at least one dose of the BNT162b2 vaccine. Efforts to estimate the true real-world effectiveness of the vaccine have been hampered by disease dynamics and social-economic discrepancies. Here, using counts of positive and hospitalized cases of vaccinated individuals, we conduct a sensitivity analysis of the vaccine effectiveness. Under an assumption of no effectiveness on the first two weeks after the 1st dose, we observe very low effectiveness on the third week. After the 2nd dose, on weeks 1 and 2 we find 73-85% effectiveness in reducing positive cases, hospitalizations, and severe cases, which increase to 89-97% effectiveness 14 days after the 2nd dose. As more granular data will be available, it will be possible to extract more exact estimates; however, the emerging evidence suggests that the vaccine is highly effective.

Introduction

Vaccination rollout in Israel of the COVID-19 vaccines started on December 20, 2020. By February 9th, 47% and 32% of the population had already received the 1st dose and 2nd dose, respectively, by the BNT162b2 vaccine developed by BioNTech and Pfizer. The vaccination campaign coincided with the beginning of a "3rd wave" of infections, and by mid-January SARS-CoV2 positive cases and hospitalizations more than doubled. To mitigate this increase in cases, on January 8 a strict lockdown was imposed. However, cases and hospitalizations did not drop as expected and as observed in previous waves. There was some frustration in the public and by government officials, and doubts were raised whether the vaccines are effective.[1]

Estimating real-world effectiveness of vaccinations is complicated compared to a randomized, controlled and double-blinded clinical trial. First, in real-world there is no control group. With the protection from the vaccine cases are eliminated, and the general population incidence does not represent the incidence rate with no vaccinations. Second, in real-world there is no randomization. Israel has seen significant discrepancies between socio-economic and demographics groups in vaccination uptake.[2] Additionally, COVID-19 disproportionately stroked individuals of lower socio-economic status. Third, the real-world vaccination is not blinded. Behavioral changes of those immunized may affect the number of encounters and chances of infection. In summary, while in the clinical trial the disease dynamics, socio-economic differences and behavioral aspects can all be controlled, in real-world, it is more complicated to accurately tease out those confounding factors.

Here, using publicly available data of COVID-19 dynamics and SARS-CoV2 positive and hospitalizations of those that were vaccinated, we provide estimates of the effectiveness of the vaccine in reducing cases, hospitalizations and severe cases due to COVID-19. All data and code used in this study are available at https://github.com/dviraran/covid_analyses.

Methods

Daily SARS-CoV2 positive cases and numbers of severe or critical hospitalization were downloaded from the Israeli Ministry of Health (MoH) COVID-19 public database.[3] Number of positives cases, hospitalizations and severe or critical hospitalizations of vaccinated individuals was provided by the MoH on February 23th, 2021. The counts are stratified by ages 60 years and above (60+) and below 60 years (60-), and five groups according to number of days from the vaccination: between day 0 to 13 of the first dose (group 1), between day 14 to 20 of the first dose (group 2), between day 0 to 6 of the 2nd dose (group 3), from day 7-13 of the 2nd dose (group 4), and from the 14+ (group 5).

To calculate vaccine effectiveness (VE), we first estimate the expected number of cases or hospitalizations (**Supplementary Figure 1**). To achieve this, we count the number of the cumulative vaccinated individuals on each day that are eligible in each group. We call this vector V(g), where g is the relevant group as described above. We then calculate the daily incidence rate of cases in the whole population. Naively, this is the number of cases divided by the population size. However, the daily incidence (d) is affected by the VE, as there are cases that are eliminated by the vaccination. To overcome this issue, we deconvolve the number of observed cases in the population per day – the number of cases from those vaccinated after the 2nd dose (S^1) and those not vaccinated or before 2nd dose (S^2). Those vaccinated are multiplied by 1 minus the VE, which provides the number of cases if they were not vaccinated. Finally, since incidence rates of the vaccinated cohort are different from the general population, we use a sensitivity parameter β to adjust for the incidence rates. Based on all this, the formula for the VE is as below:

$$(1)\ VE(g,\beta) = 1 - \frac{O(g)}{V_i(g)\cdot d_i \cdot \beta}$$

And the daily incidence d_i can be calculated by the sum of S_i^1 and S_i^2:

$$(2)\ S_i^1(\beta, VE) = V'_i \cdot d_i \cdot (1 - VE)\cdot \beta$$
$$(3)\ S_i^2 = (H - V'_i)\cdot d_i$$
$$(4)\ S_i(\beta, VE) = S_1 + S_2$$

Where $O(g)$ is the observed number of cases in the relevant group; S_i is the number of cases on day i; V'_i is the number of vaccinated individuals after the 2nd dose on day i; d_i is the daily incidence; VE is the effectiveness of the vaccine; β is the sensitivity parameter; and H is the population size (1,428,000 for >60 years old, 7,539,000 for <60 years old).

To find the solution of eq. 1 for VE, we find the value of VE by minimizing the following function, which is a combination of eq. 1 and 4:

$$(5)\ argmin_{VE}\left|1 - VE(g,\beta) - \frac{O(g)}{\sum \frac{\beta \cdot S_i(\beta,p)\cdot V_i}{H + V'_i(-1 + \beta - \beta \cdot VE(g,\beta)}}\right|$$

To estimate β for each group, we hypothesized that by day 13 of the 1st dose, there should not be an observed effect of the vaccine. We present $\pm$10% of the β values.

Results

Between December 20, 2020 and February 23th, 2021, there were 4,295,685 individuals vaccinated in Israel by the 1st dose of the BNT162b2 vaccine, of them, 1,303,244 over the age of 60 (91% of the whole 60 years and over population). By that date, 2,918,008 have already received their 2nd dose of the vaccine. Of all those vaccinated, 52,014 individuals have tested positive for SARS-CoV2, 3,148 have been hospitalized due to COVID-19 and 2,141 were hospitalized with severe or critical conditions or have died (**Table 1**).

Table 1. Number of cases of vaccinated individuals as reported by the Ministry of Health of Israel.

	Positive cases (>60y)	*Positive cases (<60y)*	*Hospitalizations (>60y)*	*Hospitalizations (<60y)*	*Severe (>60y)*	*Severe (<60y)*
1st dose, day 0-13	7,743	24,104	1,262	426	936	215
1st dose, day 14-20	5,532	8,447	826	119	595	52
2nd dose, day 0-6	1,254	1,573	171	27	132	11
2nd dose, day 7-13	1,276	1,009	196	20	137	11
2nd dose, day 14+	629	447	88	13	46	6

Based on daily numbers of vaccinations and rates of general incidence we estimated expected numbers of SARS-CoV-2 positive cases, COVID-19 hospitalizations and severe cases. We correct our estimation to two confounding factors. First, the incidence rates of those that were vaccinated early are not similar to the general population, as previous analyses have shown that older populations have lower incidence and lower socio-economic groups have higher incidence.[4] Therefore, we perform a sensitivity analysis by adjusting incidence rates using different levels of β values. Second, the general incidence rate is affected by the vaccinations, as individuals that have been vaccinated would have been infected without the vaccine. Therefore, we derived a formula that estimates the daily incidence rate by adding those eliminated cases as a function of the VE (**Methods**).

For positive cases, which are a combination of symptomatic and asymptomatic individuals, in ages 60 years and above, we find the empirical β to be 0.78, which implies that the vaccinated population are expected to have 78% the cases of the general 60+ population (**Figure 1A**). Strikingly, the analysis suggests no effect at all by day 20 of the 1st dose. However, on the 4th and 5th week, which are also weeks 1 and 2 after the 2nd dose, we observe a reduction of 73%, which increase to 96% reduction from 14+ days and above after the 2nd dose. For individuals aged below 60 years, the empirical beta values are 0.81. Here we see reduction 77% after the 2nd dose, 81% reduction in week 5, and 94% reduction from 14+ days and above after the 2nd dose (**Figure 1B**).

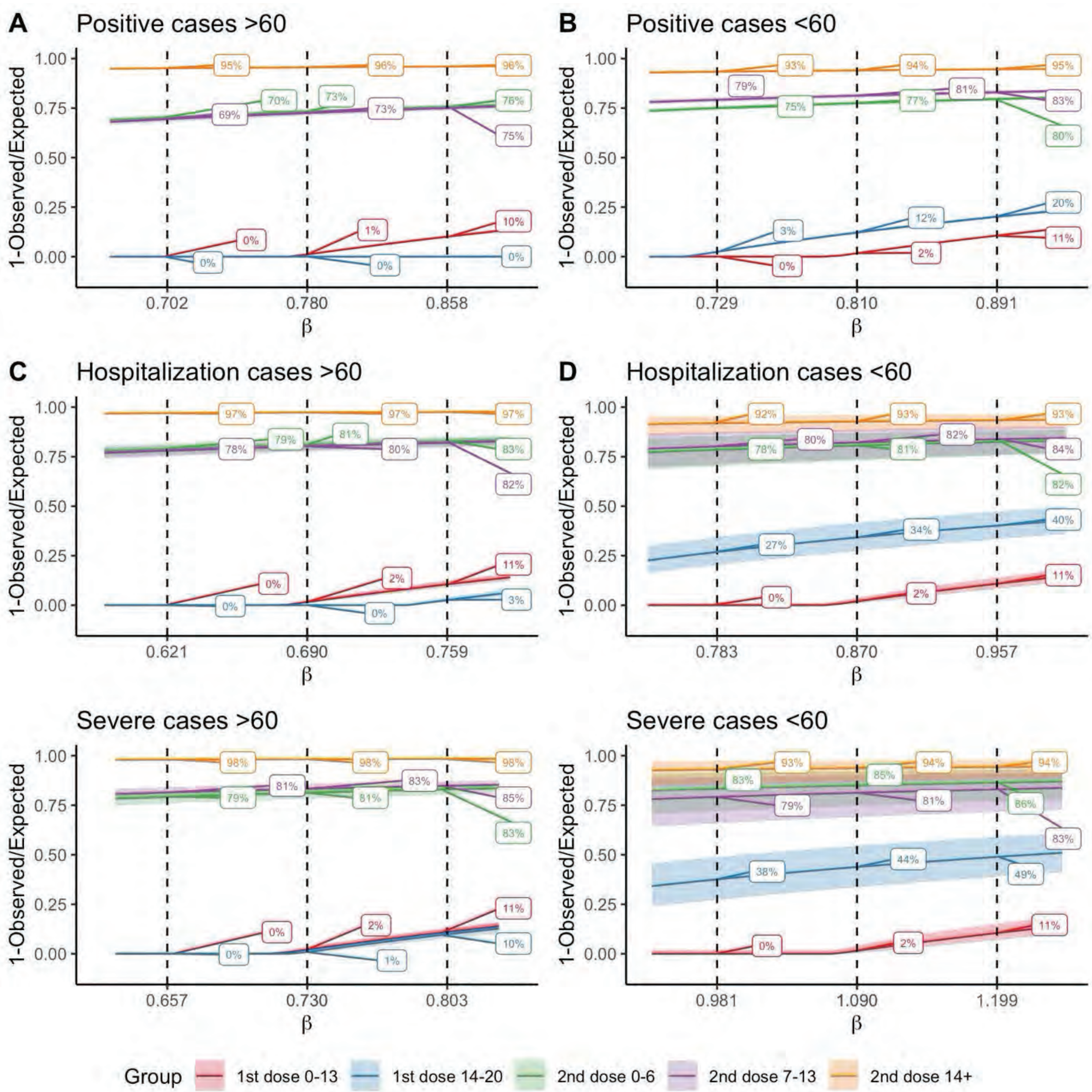

Figure 1. Effectiveness rate estimations of the vaccination by different levels of beta values. Each plot shows the estimated effectiveness (y-axis) as a function of β. Dashed lines are for empirical β value, and +-10% from the β value. 95% Confidence intervals are in shade.

Similarly, we perform the analysis for hospitalizations and severe cases, stratified by the age groups. For hospitalizations in 60+ our analysis suggests beta values of 0.69. Similarly, we do not observe any effect by day 20. After the 2nd dose we find 79-81% reduction in hospitalizations, which increase to 97% reduction two weeks after the 2nd dose (**Figure 1C**). We observe similar effectiveness in the 60- group, however with large confidence intervals, as numbers of hospitalizations are low. Interestingly, in this group we do observe low but not negligible VE of 34% in the third week (**Figure 1D**).

Finally, in severe case we estimate the β values to be between 0.73. Up to day 20 we observe no reduction in severe cases, but after the 2nd dose we observe a reduction of 81-83% in the first two weeks and 98% after day 14 (**Figure 1E**). Similar to hospitalizations, in those below age 60, the number of

severe cases is too low for a reliable estimation, but the trend is similar to the 60+ group. Again, we observe non negligible VE of 44% on the third week.

It is important to note, that while positive cases may already have been counted, hospitalizations and severe cases may deteriorate later and the number of cases is expected to increase, which in turn will reduce the estimation of the VE. To test whether this censoring affects the estimations we performed a censoring analysis on the vaccinated individuals in the group of 14+. The analysis shows that even when taking into account only those with 20+ days after the 2nd dose for calculating the expected number of cases, the VE for 60+ is still 91% for positive cases, 95% for hospitalizations and 97% for severe disease (**Supplementary Figure 2**).

Discussion

The randomized clinical trial (RCT) of BNT162b2 has suggested efficacy of 95% a week after the 2nd dose and unclear efficacy earlier.[5] It also suggested differences between the older and younger population, but with large standard errors due to relatively small sample sizes. In addition, the clinical trial was performed on a relatively small population; in contrast, by February 23th, in Israel alone 195-fold more individuals have been vaccinated compared to the trial. Therefore, real-world data VE is of high interest and important for decision-makers and mobilizing individuals to get the vaccine. Our real-world estimates are very similar to the RCT, however with a few differences. First, we do not observe any VE before the second dose. Second, full VE is only observed 14 days after the 2nd dose, and not 7 days as suggested by the RCT.

Our method adjusts for two main issues in comparing cases in vaccinated individuals and the general public. The sensitivity analysis provides VE estimates that corrects for demographic, socio-economic and additional behavioral aspects. Our deconvolution approach for correcting incidence rates allows to estimate VE in situations where the vaccine is already impactful on cases. We report here that two weeks after the 2nd dose the vaccine is over 90% effective in reducing positive cases in individuals older than 60 years, and over 95% effective in reducing hospitalizations and in preventing severe cases.

Our analysis suggest that the vaccine does not provide substantial protection in days 14-20 after the 1st dose, as we only observe substantive effectiveness in days 0-6 of the 2nd dose, which is administered in Israel on the 21st day after the 1st dose of the vaccine. We cannot differentiate here between the possibility that the 1st dose is effective but only after three weeks, or that the vaccine is only protective following the 2nd dose of the vaccine. However, there is some preliminary evidence to support that the single dose is effective after three weeks.[6]

In Israel, individuals may get tested for SARS-CoV-2 for any reason, not just due to symptoms. Thus, the positive cases come from both symptomatic and asymptomatic individuals. This is different from the clinical trial, where only symptomatic individuals with suspected COVID-19 where tested. It might explain some of the difference in effectiveness we observe in Israel regarding positive cases. The lower, VE we observe for hospitalization and severe cases may be explained by the inclusion of diverse population, including older population (the clinical trial was limited to age 85) and more comorbidities.

It is important to note that our estimates of VE in reducing the disease should not be confused with effectiveness in reducing transmission. As noted, we cannot exclude the possibility that vaccinated individuals may still get infected by SARS-CoV-2 and stay asymptomatic or with mild symptoms and will therefore not get tested. However, other studies have shown reduction in Ct values of the PCR test due to the vaccination, suggesting lower viral load, and in turn reduced transmission.[7]

Our analysis suffers from limitations. First, all analyses are performed on aggregated counts, which limits the possibilities to make individual-level inferences. Second, hospitalizations and severe cases may accumulate with time, as some of the patients will deteriorate later on. The number of new vaccinated individuals have been relatively low in the fifth week therefore this issue should not have a major effect on our estimates up to the fifth week. Third, in Israel there is an incentive to get tested if you are required to be in isolation due to contact with an infected individual, and as noted above some asymptomatic individuals are thus identified. However, this incentive is reduced for people who are 7 days after the 2nd dose, as the Israeli MOH regulations now exempts these people from mandated isolation. Thus, there is a difference in testing rates of asymptomatic individuals between groups. It is reassuring that there are relatively similar levels of effectiveness of those 7 days after the 2nd dose to those before those 7 days, suggesting that this testing incentive has only a marginal effect.

Other attempts to identify the impact of the vaccination campaign in Israel are underway. Chodik et al. compared cases in vaccinated individuals on days 13-24 after the 1st dose with vaccinated individuals in days 0-12.[8] Rossman et al. used a natural experiment approach to compare early and late vaccinated cities and differences in the prioritization for the vaccine between age groups.[4] Our contribution here is the use of the general population as a control group to assess the effectiveness rather than vaccine impact, and introducing methodological advancements to provide improved real-world estimations.

In conclusion, this study provides estimate the effectiveness of the BNT162b2 vaccine on a population level compared to the general population. Our analysis provides strong reassurance that the vaccine is highly effective. With more data that will be shared with the public we believe that more accurate estimation can be calculated.

Data and code availability

All data is public and can be downloaded from https://data.gov.il/dataset/covid-19 or Ministry of Health press releases. Data and code used in the analyses was deposited in https://github.com/dviraran/covid_analyses. In addition, we provide an interactive shiny app, which will be updated as more data is available by the Ministry of Health - https://dviraran.shinyapps.io/VaccineEffectIsrael/.

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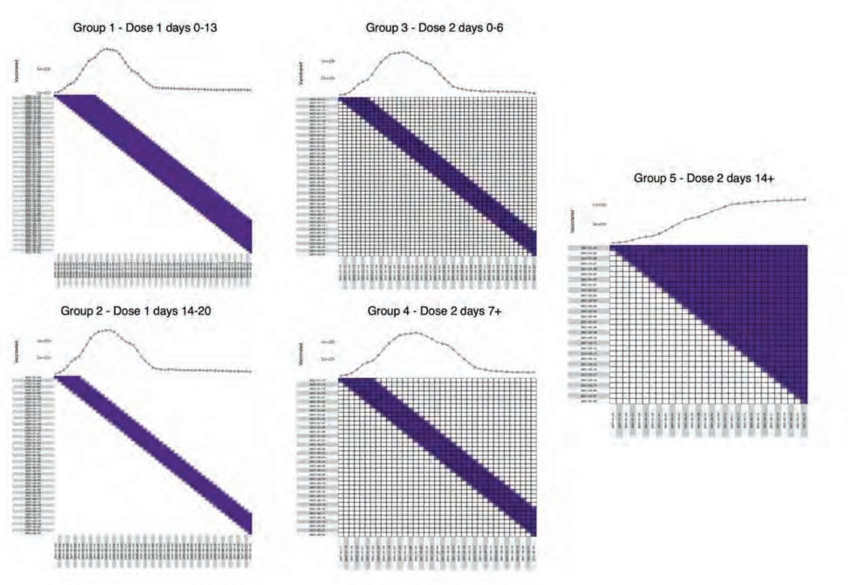
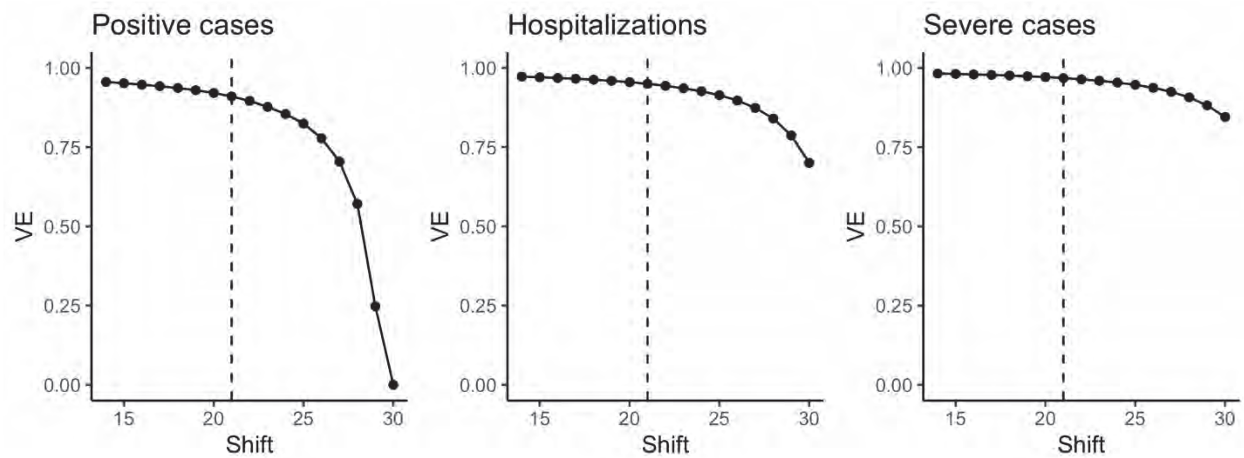
Supplementary Figures

Supplementary Figure 1. Visualization of expected case counts model. Days counted from vaccination. Columns are days of vaccination; Rows are days of possible infection. A cell is blue if the vaccinated individual is counted in the relevant group. The distribution on the top is the sum of each column (the number of vaccinated individuals that are counted for that date). Note that in group 5 numbers are steadily increasing, and most cases are recent, thus, hospitalizations and severe cases are expected to increase.



Supplementary Figure 2. Censoring analysis for 14+ days after 2nd dose group. Vaccine effectiveness is calculated using observed counts of 14+ days after 2nd dose, however, expected

counts are calculated using those vaccinated only after number of days in the x-axis. This analysis allows to estimate VE only for those with sufficient time to deteriorate to severe disease.



Expanding COVID-19 Response in Rural Communities through Rural Health Clinics

To expand access to vaccines and ensure equity in COVID-19 response in rural communities, the Health Resources and Services Administration is working with Rural Health Clinics (RHCs) across the nation to strengthen vaccine allocation and confidence, and to expand COVID-19 testing and mitigation.

RHCs are a special certification given to health care practices in underserved rural areas by the Centers for Medicare and Medicaid Services (CMS). More than 4,600 Rural Health Clinics (RHCs) in 45 states make up a key part of the rural health care infrastructure and help address health equity gaps in medically underserved rural communities to improve health outcomes for rural residents.

Rural Health Clinic (RHC) COVID-19 Programs

In response to the coronavirus pandemic, three new programs are available to help RHCs meet community needs and improve rural health care services:

Expanding COVID-19 Testing and Mitigation

- Rural Health Clinic COVID-19 Testing and Mitigation (RHCCTM) Program will help RHCs maintain and increase testing levels and establish and expand mitigation activities tailored to local community needs. The program builds upon HRSA's Rural Health Clinic COVID-19 Testing Program.

Ensuring Equitable Distribution of Vaccines in Rural Areas

- Rural Health Clinic Vaccine Distribution (RHCVD) Program was launched in partnership with the Centers for Disease Control and Prevention (CDC). Under the program, enrolled Medicare-certified RHCs will receive direct COVID-19 vaccines in addition to their normal jurisdictions' weekly allocation.

Building Vaccine Confidence

- Rural Health Clinic Vaccine Confidence (RHCVC) Program supports outreach efforts to increase vaccinations in rural communities. More than 1,980 RHCs are using these resources to promote vaccine confidence and work to get more people vaccinated and protected from COVID-19 in medically underserved rural communities.

Resources

- RHIhub - Rural Health Clinics (RHCs)
- Rural Health Clinics and Federal Office of Rural Health Policy (FORHP) Rural Health Areas (Map) (PDF - 1.7 MB)
- Medicare Learning Network - Rural Health Clinic Fact Sheet (PDF - 805 KB)
- National Association of Rural Health Clinics (NARHC)

Contacts

For additional questions related The RHC COVID-19 Testing or Testing and Mitigation Program:
RHCCOVID-19Testing@hrsa.gov.

The RHC COVID-19 Vaccine Distribution Program:
RHCVaxDistribution@hrsa.gov.

The RHC Vaccine Confidence Program:
RHCVaxConfidence@hrsa.gov.

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Experiences of Home Health Care Workers in New York City During the Coronavirus Disease 2019 Pandemic
A Qualitative Analysis

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IMPORTANCE Home health care workers care for community-dwelling adults and play an important role in supporting patients with confirmed and suspected coronavirus disease 2019 (COVID-19) who remain at home. These workers are mostly middle-aged women and racial/ethnic minorities who typically earn low wages. Despite being integral to patient care, these workers are often neglected by the medical community and society at large; thus, developing a health care system capable of addressing the COVID-19 crisis and future pandemics requires a better understanding of the experiences of home health care workers.

OBJECTIVE To understand the experiences of home health care workers caring for patients in New York City during the COVID-19 pandemic.

DESIGN, SETTING, AND PARTICIPANTS From March to April 2020, a qualitative study with 1-to-1 semistructured interviews of 33 home health care workers in New York City was conducted in partnership with the 1199SEIU Home Care Industry Education Fund, a benefit fund of the 1199 Service Employees International Union United Healthcare Workers East, the largest health care union in the US. Purposeful sampling was used to identify and recruit home health care workers.

MAIN OUTCOMES AND MEASURES Audio-recorded interviews were professionally transcribed and analyzed using grounded theory. Major themes and subthemes were identified.

RESULTS In total, 33 home health care workers employed by 24 unique home care agencies across the 5 boroughs of New York City participated. Participants had a mean (SD) age of 47.6 (14.0) years, 32 (97%) were women, 21 (64%) were Black participants, and 6 (18%) were Hispanic participants. Five major themes emerged: home health care workers (1) were on the front lines of the COVID-19 pandemic but felt invisible; (2) reported a heightened risk for virus transmission; (3) received varying amounts of information, supplies, and training from their home care agencies; (4) relied on nonagency alternatives for support, including information and supplies; and (5) were forced to make difficult trade-offs in their work and personal lives.

CONCLUSIONS AND RELEVANCE In this qualitative analysis, home health care workers reported providing frontline essential care, often at personal risk, during the COVID-19 pandemic. They experienced challenges that exacerbated the inequities they face as a marginalized workforce. Interventions and policies to better support these frontline health care professionals are urgently needed.

Invited Commentary page 1459

Author Audio Interview

Supplemental content

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The illness caused by the novel severe acute respiratory syndrome coronavirus 2 infection, coronavirus disease 2019 (COVID-19), was first reported in New York City (NYC) at the beginning of March.[1] Two months later, the US surpassed 1 million diagnosed cases, with NYC reporting one-third of these cases and more than 20 000 deaths.[2] Home health care workers, who are composed of home health and personal care aides and home attendants, care for community-dwelling adults and therefore play an important role in supporting those with confirmed and suspected COVID-19 who remain at home.[3-5] Unlike other health professionals, whose interactions with patients are relatively brief, home health care workers spend hours to days with patients, assisting with activities of daily living (eg, bathing and dressing), instrumental activities of daily living (eg, preparing meals and cleaning), and medically oriented tasks (eg, vital signs and wound care). In addition, these workers frequently provide companionship and emotional support.[6] The COVID-19 pandemic brings many potential challenges to this caregiving role given the risk of virus transmission to both patients and workers in the community.

Despite being integral to patient care, home health care workers—who are mostly middle-age women, people of color, and immigrants—are often an invisible and vulnerable workforce.[5,7] They work long hours, earn minimum wages, and have limited opportunities for career advancement.[8,9] Indeed, 1 of every 6 workers lives below the federal poverty line.[5] These conditions have led to high turnover rates and workforce shortages.[10,11] As the COVID-19 pandemic escalates and as home health care workers continue to care for elderly patients and for medically complex patients in the home, it is likely that this workforce will become increasingly more vulnerable, both physically and financially.

In this context, the present study aimed to understand the experiences of home health care workers caring for patients in NYC during the COVID-19 pandemic because, to date, the majority of studies and lay press articles have focused on the experiences of hospital-based health care professionals and employees. Specifically, we sought to elucidate the challenges home health care workers face regarding disease transmission, preparedness, and well-being, to inform future studies, interventions, and policies.

Key Points

Question What are the experiences of home health care workers caring for older adults and for patients with chronic illnesses during the coronavirus disease 2019 (COVID-19) pandemic?

Findings In this qualitative study of 33 home health care workers employed by 24 unique home care agencies across New York City, participants reported that they were at heightened risk for contracting and transmitting COVID-19. Despite providing integral care to vulnerable patients, home health care workers felt inadequately supported and generally invisible.

Meaning During the COVID-19 pandemic, home health care workers experienced challenges that increased their vulnerability as a workforce.

Methods

Setting and Study Population

This qualitative study was conducted from March 26 to April 30, 2020, in partnership with a benefit fund of the 1199 Service Employees International Union (SEIU) United Healthcare Workers East, the 1199SEIU Home Care Industry Education Fund (hereafter called the Education Fund). The 1199SEIU is the largest health care union in the US, representing more than 400 000 workers in hospitals, nursing homes, clinics, and home care agencies.[12] The Education Fund provides education and training benefits to 75 000 home health care workers employed by 55 home care services agencies in NYC.[13] We used purposeful sampling to achieve a balanced sample of home health care workers with respect to their agency (range of sizes of certified and licensed home care agencies) and borough of employment in NYC.[14] To be eligible, workers had to be currently employed by a home care agency in NYC and speak English. Using a standardized script, Education Fund staff members conducted general outreach via telephone calls among home health care workers who had in-person training courses at the Education Fund headquarters that needed to be rescheduled given the COVID-19 pandemic. During these calls, staff assessed workers for their interest and eligibility. The lead investigator (M.R.S.) then approached these individuals via email or telephone with a standardized script explaining the details of this voluntary study. To ensure even more perspectives, the lead investigator conducted written outreach to a few agencies (affiliated with the Education Fund) that represented additional geographic diversity and whose workers had not yet been included in the sample. This article adheres to the Consolidated Criteria for Reporting Qualitative Research (COREQ) reporting guideline.[15] The study was approved by the Cornell University institutional review board. Participants provided verbal informed consent—because interviews were not conducted in person for safety during the COVID-19 pandemic—including permission to record the interview and to publish deidentified excerpts from the interview. Informed consent was obtained in a manner consistent with the Common Rule requirement. Following the interview, participants received $25.00 gift cards.

Data Collection

Three researchers (M.R.S., E.T., and A.P.) trained in qualitative methods conducted 1-to-1 interviews using a semistructured topic guide and Zoom video conference software.[16] The topic guide was informed by prior research conducted by members of our team,[7,17,18] informal discussions with agency leaders at the beginning of the pandemic, and prior studies on home care workers' preparedness during past epidemics.[19-21] Interview questions broadly focused on (1) what workers knew about COVID-19; (2) how COVID-19 affected their work; and (3) the challenges they experienced during COVID-19 (eAppendix 1 in the Supplement). In addition, self-reported demographic characteristics data, including age, sex, race/ethnicity, educational level, and employment history, were collected.

Table. Demographic Characteristics of 33 Participants[a]

Characteristic	No. (%)
Age, mean (SD), y	47.6 (14.0)
Female sex	32 (97)
Race/ethnicity	
White	3 (9)
Black	21 (64)
Hispanic	6 (18)
Asian	2 (6)
Mixed or other	1 (3)
Educational level	
<High school	3 (9)
Completed high school or GED	8 (24)
Some college	9 (27)
College or more	13 (39)
Mean (SD) No. of years as home health care worker	10.9 (7.0)
No. of (unique) home care agencies	24
Self-reported suspected or confirmed COVID-19	4 (12)

Abbreviations: COVID-9, coronavirus disease 2019; GED, General Educational Development.

[a] Data were self-reported using open-ended questions. Responses for sex, race/ethnicity, and educational level were subsequently categorized (as shown).

Figure. Geographic Map of New York City and the Locations of the Home Care Agencies in Which Participants Were Employed

Each star represents the headquarters of a home care agency from which participants in the study were employed. Some agencies had more than 1 headquarters. JFK indicates John F. Kennedy.

Data Analysis

Interviews were audio recorded and professionally transcribed. Data were analyzed using grounded theory.[22,23] To ensure rigor of the method, a constant comparative approach was used at each stage. First, 3 investigators (E.T., A.P., and J.C.) independently reviewed and open coded 3 transcripts. Data were analyzed in Excel spreadsheets, and codes were analyzed using a custom-built and Python-based visualization tool.[24] The preliminary coding schema totaled 91 codes. Two lead investigators (M.R.S. and N.D.) reviewed the first 3 transcripts and consolidated the preliminary codes into a final codebook of 66 unique codes (eAppendix 2 in the Supplement). The 3 investigators then recoded these 3 transcripts using the uniform codebook and subsequently applied it to remaining transcripts. The 3 coders met to revise the codebook every 2 transcripts, and the 2 lead investigators reviewed each version of the codebook. Saturation, that is, the point at which no new codes were added, was achieved at the 25th interview. We conducted 8 additional interviews beyond saturation because these participants were already scheduled and had rearranged their work schedules to participate.

Once coding of all interviews was completed, the 5-person team (M.R.S., E.T., A.P., J.C., and N.D.) consolidated the codes into 19 categories by consensus.[25] The team then iteratively consolidated these categories into unifying themes, reconciling discrepancies by discussion.[26] Themes were further refined by team members (A.C.A., L.M.K., and C.K.A.) who had not conducted or coded interviews but who had content expertise.

Results

In total, 33 home health care workers employed by 24 unique home care agencies across 5 boroughs of NYC participated (**Table**). Participant mean (SD) age was 47.6 (14.0) years, 32 (97%) were women, 21 (64%) were Black participants, 6 (18%) were Hispanic participants, and 22 (67%) completed some college or more education. Overall, participants had a mean (SD) of 10.9 (7.0) years of experience as home health care workers. Of 33 participants, 4 (12%) reported that they had become ill with suspected or confirmed COVID-19 during the study period and that they had stopped working once they experienced symptoms. The **Figure** shows the geographic distribution of the 24 agencies that employed the participants. Interview duration ranged from 25 to 40 minutes. The analysis resulted in 5 major themes with subthemes (**Box**). We present them alongside representative quotations.

Theme 1: On the Front Lines of COVID-19 Medical Management, but Invisible

Participants reported that they were considered essential workers in NYC. As such, they continued to work and care for their patients despite social distancing policies that would otherwise require keeping people 6 feet apart. Participants reported that the majority of their patients had several chronic conditions, which rendered patients high risk for COVID-19. In addition to their normal caregiving tasks, the participants also monitored patients for COVID-19 symptoms. This process presented new challenges because symptoms, such as cough and shortness of breath, often mimicked patients' usual symptoms. When concern for the potential of COVID-19 arose, participants acted; some participants called their agency, whereas others called the patients' physicians and some called 911.

Box. Major Themes and Subthemes Summarizing Home Health Care Workers' Experiences When Caring for Patients During the Coronavirus Disease 2019 (COVID-19) Pandemic

Theme 1: On the Front Lines of COVID-19 Medical Management, but Invisible

Subthemes
- Providing day-to-day care for patients with chronic conditions
- Monitoring patients for COVID-19 symptoms
- Taking precautions to prevent COVID-19 in the home
- Feeling invisible

Theme 2: Heightened Risk for COVID-19 Transmission to Patients and Themselves

Subthemes
- Risk of transmitting COVID-19 to patients
- Risk of contracting COVID-19 themselves
- Reliance on public transportation, which increases exposure risk
- Numerous home care workers per patient, increases risk of spread

Theme 3: Varying Levels of Support From Agencies, Including Information and Personal Protective Equipment

Subthemes
- Differing amounts of COVID-19 information
- Limited personal protective equipment
- Lacking COVID-19–specific training

Theme 4: Reliance on Alternative Sources for Support

Subthemes
- Information sources included news media, social media, and others
- Nonagency sources of personal protective equipment
- Peer support

Theme 5: Forced to Make Tough Trade-offs Between Their Own Health and Finances

Subthemes
- Working vs risk of exposure
- Working vs risk of losing wages and benefits
- Risk of transmission vs duty to provide care

"I will ask them how long they had the cough. . . . I know even with a cough, you can't go to an ER [emergency room]. . . . So I will call the doctor, who will give us information. Then I will try to do that for the patient and myself."

Beyond monitoring their patients' physical symptoms, participants also tried to assist with their patients' emotional health. Many reported that this endeavor was worsened by patients watching the news.

"It's become a very stressful environment. She watches the news constantly. . . . As soon as I set foot in the door—'did you see this, did you see that, about coronavirus?'"

In addition, participants went to great lengths to take COVID-19 precautions while in patients' homes. They described engaging in elaborate cleaning routines whenever possible during their shifts.

"I clean like there's no tomorrow. I wipe down every surface—the table—the chair. I walk with the little bleach wipes."

However, despite these efforts to keep their patients healthy and safe, many described feeling invisible to the health care community and society.

"We're definitely a forgotten field. . . . You hear people clapping, thanking doctors and nurses, even the hospital cleaning staff. . . . I'm not doing this because I want praise; I love what I do. But it would be nice for people to show us gratitude."

Theme 2: Heightened Risk for COVID-19 Transmission to Patients and Themselves

Participants explained that providing care to patients placed them in a unique position with respect to COVID-19 transmission. They worried about their patients becoming ill in general and about transmitting the virus to them.

"I feel guilty because since they're not going outside, I know if they catch it, it's because of me. That's my fear going to work."

To protect patients, participants went to the grocery store and pharmacy on their behalf, which increased their own risk for contracting COVID-19. Although sometimes they volunteered, other times they were asked.

"He needs to stay inside the house, so he tells me, 'I need you to go there, go here.' I really don't want to, but I can't say no. I'm the aide; I'm supposed to do this."

Participants also worried about their own risk of contracting COVID-19, and nearly all felt that their dependence on public transportation increased this risk. Many participants reported using public transportation to get to their patients' homes, to run errands for them, and to travel to their agency for supplies.

"I take 3 buses to get to work: the 9, the 19, and the 5. . . . That's a lot of traveling and different people around."

Finally, many participants cared for a patient alongside other workers who entered and left the home each day. This added to their fear of transmitting COVID-19 to their patients and to one another.

"There are 5 of us that work with her. . . . What happens if we all get sick?"

Owing to this concern, some participants tried to coordinate hygiene and handoff practices with the other aides caring for common patients.

Theme 3: Varying Levels of Support From Agencies, Including Information and Personal Protective Equipment

Participants described receiving varying levels of support from their agencies, specifically regarding receiving information about COVID-19, the availability of personal protective equipment (PPE), and receiving COVID-19 training. Although some agencies adapted quickly to the pandemic by providing workers with COVID-19–related information on a weekly or daily basis, others reportedly barely communicated about the pandemic.

"Nobody ever told us, 'you gotta take precautions' and blah blah; nobody tell us anything."

Many home health care workers also reported that they lacked adequate PPE from their agencies, including masks and gloves, which they felt was essential for care.

"I'm worried about getting infected because I don't have the right equipment. The agency has not really been providing for their workers, at all."

Participants reported that they had not received COVID-19-specific training from their agencies but had hoped that it would be offered in the future. Some agencies asked participants to perform daily "self-assessments." Self-assessments, which were usually automated by phone, were intended to screen home health care workers for COVID-19 symptoms. Depending on how they answered, workers would be encouraged to go to work or to call their doctor.

"They text a 4-question screener every day. They want to know if something changes in your body. Do you have a fever? Do you have a cough?"

Theme 4: Reliance on Alternative Sources for Support

Owing to varying levels of institutional support, participants often relied on others for information and help. For example, if their agency did not provide information on COVID-19, participants turned to the news media, social media, government briefings, and their worker union.

"I watch the television, the news. I listen. I read on my phone, like on Facebook. I try to read about it everywhere."

Although some agencies did provide PPE, many participants felt that the amount supplied was insufficient to meet their daily patient care needs. In response, some participants purchased their own supplies or turned to family members and friends.

"I don't think we should have to go out and buy masks. I spent $20.00 to get a box of masks. . . . I walk all over just to buy a small can of Lysol for $7.00."

Some participants also relied on other home health care workers for advice and support or turned to religion.

"We talk to each other. We need to protect ourselves for the clients, if you want to keep working."

Theme 5: Forced to Make Tough Trade-offs Between Their Own Health and Finances

Owing to these challenges, participants described constantly navigating hard choices. For example, when patients contracted COVID-19, workers had to decide whether to continue caring for them, which meant potentially exposing themselves. Sometimes, however, patients fearful of contracting COVID-19 declined home care services, leaving workers to decide whether they should accept a new patient who they did not know. Workers also weighed whether they should remove themselves from cases they perceived to be risky. Taken together, they tried balancing the risks of work with their own health and financial well-being.

"You have to contribute certain hours to get benefits. . . . I have to go out there because I have bills to pay."

"It's just not a job where you can work from home."

In addition, many spoke about balancing the risks of caring for patients during the COVID-19 pandemic with the duty or "calling" they felt to help patients.

"I see a fire. Am I going to walk right into that fire? . . . If I have the backup, the proper gear, yes, I'm going to be there on the front lines to help that person."

Discussion

To our knowledge, this is the first study to describe home health care workers' experiences caring for older adults and for persons with chronic health conditions in the home during the COVID-19 pandemic. Our findings suggest that, although these study participants acted as essential health care professionals, they often felt poorly supported and generally invisible. Not only were they caring for a vulnerable patient population, but, owing to shortages in PPE and a heavy reliance on public transportation, they were at high risk for contracting COVID-19 and for transmitting it to their patients, other workers, and their own families. However, many could not afford to stop working, and others continued working out of a sense of duty. Taken together, caring for patients during the COVID-19 pandemic exacerbated this workforce's existing vulnerabilities and professional challenges.

Another key finding was that, across all 5 themes, home health care workers expressed feelings of anxiousness stemming from numerous stressors. As health care professionals, they feared what the virus could do to their patients and to themselves. As marginalized workers, however, they also feared the economic toll the virus might have on their ability to maintain their pay and benefits. Prior studies have found that, even before the COVID-19 pandemic, home health care workers endured high levels of stress and job insecurity.[27,28] The additional strain placed on workers by the pandemic, coupled with their already tenuous standing as minimum wage workers, exacerbated this stress. Our findings suggest that additional efforts to support workers' mental and physical well-being during the pandemic are needed. Encouragingly, the 1199SEIU is now offering well-being and resiliency training for this workforce.[29]

Some of the trade-offs that home health care workers have navigated during the COVID-19 pandemic are similar to those faced by other health care professionals, but other challenges are unique and warrant separate attention from government officials and policy makers. First, although hospitals initially experienced PPE shortages,[30,31] supplies in many regions of the United States have generally improved. Agencies, on the other hand, remain understocked. Indeed, a survey conducted by the Home Care Association of New York found that 67% of home care and hospice agencies in NY do not have sufficient PPE.[32] Given that the number of cases is expected to rise, legislation that makes PPE available to home care agencies is critical. Second, the financial hardships that workers have endured point to the need for them to be considered "essential workers" across the US, a designation that they already have in NY. Without such designation, workers cannot receive benefits, such as paid sick leave and childcare, during the pandemic.[33] Third, whereas hospitals have communicated COVID-19 information to clinicians and staff regularly, such information provided to home health workers has varied by agency, which may reflect uncertainty with respect to guidelines in the long-term care sector. To address this situation, unions

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and some agencies have recently added COVID-19 information to websites and (virtual) town halls.[13] Our findings suggest that an approach integrating this information alongside COVID-19-specific training needs to be systematically implemented. Fourth, policies at the agency level that geographically organize cases to minimize public transportation use are important to protect home health workers and patients from community spread.

Strengths and Limitations

The strengths of our study include our community-partnered approach to recruit a diverse sample of participants employed by 24 unique home care agencies across NYC. In addition, we analyzed the data using a rigorous, grounded theory approach. We also note limitations. Because this is a qualitative study, the findings are not generalizable but rather convey experiences of participants that may not be captured in quantitative investigations. In addition, owing to our sample's composition, our findings may not reflect the experiences of nonunionized or privately hired workers, non-English speakers, and those in suburban or rural areas. Finally, this study does not include the perspectives of the home care agency leadership or other stakeholders in home care; future research should elicit these perspectives.

Conclusions

Home health care workers have been on the front lines, working to ensure the health of older adults and those with chronic conditions or disabilities during the COVID-19 pandemic. In doing so, these workers are at considerable risk for contracting COVID-19 themselves. The risk of contracting COVID-19 has been exacerbated by inconsistent delivery of information on what home care workers should do to protect themselves and their clients, inadequate PPE, and a heavy reliance on public transportation. Already a vulnerable workforce, home health care workers face additional risks to their physical, mental, and financial well-being during the COVID-19 pandemic. Interventions and policies are urgently needed to protect this workforce and the vital role that they play.

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Invited Commentary

Extreme Vulnerability of Home Care Workers During the COVID-19 Pandemic—A Call to Action

Theresa A. Allison, MD, PhD; Anna Oh, PhD, MPH, RN; Krista L. Harrison, PhD

Coronavirus disease 2019 (COVID-19) has been identified in more than 14 000 US nursing homes and other long-term care settings.[1] More than 316 000 residents and staff members have contracted COVID-19, and they account for 57 000 of more than 140 000 deaths in the US.[1,2] Despite our recognition of the higher mortality rates among older adults and higher overall rates of disease among nursing home staff,[3] we still know little about the risks and experiences of workers who provide help and care to older adults who live at home. Home health aides, personal care aides, and home attendants (hereafter referred to as home care workers[4]) are members of a vulnerable population within health care delivery. Underpaid and overwhelmingly women of color, they shoulder the responsibility for hands-on assistance with bathing, toileting, dressing, and housekeeping for vulnerable older adults in the home.[5] Home care workers are essential to the health of more than 7 million older adults who require care in the home.[6,7]

Author Audio Interview

Related article page 1453

In this issue of *JAMA Internal Medicine*, Sterling and colleagues[8] present the findings from in-depth interviews with 33 unionized home care workers (64% Black/African American participants, 18% Latinx/Hispanic participants, and 97% women) across the 5 boroughs of New York City. Thanks to the quick leveraging of relationships between a medical school and a union chapter, the highly efficient use of a skilled qualitative research team, and meticulous inductive qualitative analysis, the authors have provided a window into the vulnerability of home care workers during the COVID-19 pandemic. This is a necessary step toward a robust evidence base on the clinical, educational, and support needs of these health care workers. These findings are prerequisite to improving the health and well-being of home care workers during future pandemics and outbreaks.

The findings are alarming but not surprising to those who are familiar with the work of home care workers. Sterling et al[8] identify the perils of working on the front lines of the New York City epidemic while remaining publicly and privately invisible, including an absence of public recognition and a lack of resources for reducing COVID-19 transmission. The authors provide a glimpse into the concerns of home care workers, showing how daily, face-to-face, hands-on work with care recipients increases the risk of transmission for both home care workers and care recipients during each home visit. Some home care workers had more support from their agencies, while others had little training on the epidemic; inconsistencies in levels of support led to a dangerous lack of knowledge. In particular, home care workers faced shortages in the personal protective equipment (PPE) needed to prevent COVID-19 transmission in home-based health care. Although lack of sufficient PPE has been widespread throughout the first few months of the pandemic in the United States, inadequate PPE in the home increases transmission risks for not only the home health worker and care recipient but also other household members and visitors. As creative professionals, home care workers reported seeking alternative sources of information and equipment. They discussed navigating difficult decisions about risks to their own health (by working) and finances (by not working) and their concerns about the effects of those decisions on care recipients. With 12% of this small sample self-reporting suspected or confirmed COVID-19 in themselves, they also made transparent the magnitude of their vulnerability to transmission of severe acute respiratory syndrome coronavirus 2 during the COVID-19 pandemic. Their stories provide some of

FDA NEWS RELEASE

FDA Approves First COVID-19 Vaccine

Approval Signifies Key Achievement for Public Health

For Immediate Release:

August 23, 2021

Español (https://www.fda.gov/news-events/press-announcements/la-fda-aprueba-la-primera-vacuna-contra-el-covid-19)

Today, the U.S. Food and Drug Administration approved the first COVID-19 vaccine. The vaccine has been known as the Pfizer-BioNTech COVID-19 Vaccine, and will now be marketed as Comirnaty (koe-mir'-na-tee), for the prevention of COVID-19 disease in individuals 16 years of age and older. The vaccine also continues to be available under emergency use authorization (EUA), including for individuals 12 through 15 years of age and for the administration of a third dose in certain immunocompromised individuals.

"The FDA's approval of this vaccine is a milestone as we continue to battle the COVID-19 pandemic. While this and other vaccines have met the FDA's rigorous, scientific standards for emergency use authorization, as the first FDA-approved COVID-19 vaccine, the public can be very confident that this vaccine meets the high standards for safety, effectiveness, and manufacturing quality the FDA requires of an approved product," said Acting FDA Commissioner Janet Woodcock, M.D. "While millions of people have already safely received COVID-19 vaccines, we recognize that for some, the FDA approval of a vaccine may now instill additional confidence to get vaccinated. Today's milestone puts us one step closer to altering the course of this pandemic in the U.S."

Since Dec. 11, 2020, the Pfizer-BioNTech COVID-19 Vaccine has been available under EUA in individuals 16 years of age and older, and the authorization was expanded to include those 12 through 15 years of age on May 10, 2021. EUAs can be used by the FDA during public health emergencies to provide access to medical products that may be effective in preventing, diagnosing, or treating a disease, provided that the FDA determines that the known and potential benefits of a product, when used to prevent, diagnose, or treat the disease, outweigh the known and potential risks of the product.

FDA-approved vaccines undergo the agency's standard process for reviewing the quality, safety and effectiveness of medical products. For all vaccines, the FDA evaluates data and information included in the manufacturer's submission of a biologics license application (BLA). A BLA is a

comprehensive document that is submitted to the agency providing very specific requirements. For Comirnaty, the BLA builds on the extensive data and information previously submitted that supported the EUA, such as preclinical and clinical data and information, as well as details of the manufacturing process, vaccine testing results to ensure vaccine quality, and inspections of the sites where the vaccine is made. The agency conducts its own analyses of the information in the BLA to make sure the vaccine is safe and effective and meets the FDA's standards for approval.

Comirnaty contains messenger RNA (mRNA), a kind of genetic material. The mRNA is used by the body to make a mimic of one of the proteins in the virus that causes COVID-19. The result of a person receiving this vaccine is that their immune system will ultimately react defensively to the virus that causes COVID-19. The mRNA in Comirnaty is only present in the body for a short time and is not incorporated into - nor does it alter - an individual's genetic material. Comirnaty has the same formulation as the EUA vaccine and is administered as a series of two doses, three weeks apart.

"Our scientific and medical experts conducted an incredibly thorough and thoughtful evaluation of this vaccine. We evaluated scientific data and information included in hundreds of thousands of pages, conducted our own analyses of Comirnaty's safety and effectiveness, and performed a detailed assessment of the manufacturing processes, including inspections of the manufacturing facilities," said Peter Marks, M.D., Ph.D., director of FDA's Center for Biologics Evaluation and Research. "We have not lost sight that the COVID-19 public health crisis continues in the U.S. and that the public is counting on safe and effective vaccines. The public and medical community can be confident that although we approved this vaccine expeditiously, it was fully in keeping with our existing high standards for vaccines in the U.S."

FDA Evaluation of Safety and Effectiveness Data for Approval for 16 Years of Age and Older

The first EUA (https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19), issued Dec. 11, for the Pfizer-BioNTech COVID-19 Vaccine for individuals 16 years of age and older was based on safety and effectiveness data (https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19) from a randomized, controlled, blinded ongoing clinical trial of thousands of individuals.

To support the FDA's approval decision today, the FDA reviewed updated data from the clinical trial which supported the EUA and included a longer duration of follow-up in a larger clinical trial population.

Specifically, in the FDA's review for approval, the agency analyzed effectiveness data from approximately 20,000 vaccine and 20,000 placebo recipients ages 16 and older who did not have evidence of the COVID-19 virus infection within a week of receiving the second dose. The safety of Comirnaty was evaluated in approximately 22,000 people who received the vaccine and 22,000 people who received a placebo 16 years of age and older.

Based on results from the clinical trial, the vaccine was 91% effective in preventing COVID-19 disease.

More than half of the clinical trial participants were followed for safety outcomes for at least four months after the second dose. Overall, approximately 12,000 recipients have been followed for at least 6 months.

The most commonly reported side effects by those clinical trial participants who received Comirnaty were pain, redness and swelling at the injection site, fatigue, headache, muscle or joint pain, chills, and fever. The vaccine is effective in preventing COVID-19 and potentially serious outcomes including hospitalization and death.

Additionally, the FDA conducted a rigorous evaluation of the post-authorization safety surveillance data pertaining to myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine and has determined that the data demonstrate increased risks, particularly within the seven days following the second dose. The observed risk is higher among males under 40 years of age compared to females and older males. The observed risk is highest in males 12 through 17 years of age. Available data from short-term follow-up suggest that most individuals have had resolution of symptoms. However, some individuals required intensive care support. Information is not yet available about potential long-term health outcomes. The Comirnaty Prescribing Information includes a warning about these risks.

Ongoing Safety Monitoring

The FDA and Centers for Disease Control and Prevention have monitoring systems in place to ensure that any safety concerns continue to be identified and evaluated in a timely manner. In addition, the FDA is requiring the company to conduct postmarketing studies to further assess the risks of myocarditis and pericarditis following vaccination with Comirnaty. These studies will include an evaluation of long-term outcomes among individuals who develop myocarditis following vaccination with Comirnaty. In addition, although not FDA requirements, the company has committed to additional post-marketing safety studies, including conducting a pregnancy registry study to evaluate pregnancy and infant outcomes after receipt of Comirnaty during pregnancy.

The FDA granted this application Priority Review (https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review). The approval was granted to BioNTech Manufacturing GmbH.

Related Information

- Comirnaty Prescribing Information (http://www.fda.gov/vaccines-blood-biologics/comirnaty)
- Cormirnaty and Pfizer-BioNTech COVID-19 Vaccine | FDA (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine)

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Fear and avoidance of healthcare workers: An important, under-recognized form of stigmatization during the COVID-19 pandemic

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ABSTRACT

Background: During past disease outbreaks, healthcare workers (HCWs) have been stigmatized (e.g., shunned, ostracized) by members in their community, for fear that HCWs are sources of infection. There has been no systematic evaluation of HCW stigmatization during the COVID-19 pandemic.
Methods: Non-HCW adults from the United States and Canada (N = 3551) completed an online survey, including measures of HCW stigmatization, COVID Stress Syndrome, and avoidance.
Results: Over a quarter of respondents believed that HCWs should have severe restrictions placed on their freedoms, such as being kept in isolation from their communities and their families. Over a third of respondents avoided HCWs for fear of infection. Participation in altruistic support of HCWs (i.e., evening clapping and cheering) was unrelated to stigmatizing attitudes. Demographic variables had small or trivial correlations with HCW stigmatization. People who stigmatized HCWs also tended to avoid other people, avoid drug stores and supermarkets, and avoid leaving their homes. Factor analysis suggested that HCW stigmatization is linked to the COVID Stress Syndrome.
Conclusion: Fear and avoidance of HCWs is a widespread, under-recognized problem during the COVID-19 pandemic. It is associated with the COVID Stress Syndrome and might be reduced by interventions targeting this syndrome.

1. Introduction

Being the target of stigmatization is stressful (Goffman, 1963). During widespread outbreaks of infectious disease, healthcare workers (HCWs) are often stigmatized by people in their communities; that is, HCWs have been feared, avoided, shunned, or ostracized due to public fear that HCWs are sources of infection (Bagcchi, 2020; Taylor, 2019). To illustrate, during the 2003 outbreak of Severe Acute Respiratory Syndrome (SARS), in studies conducted in Taiwan and Hong Kong, 20–49 % of HCWs involved in the care of SARS patients reported being shunned, avoided, or otherwise stigmatized by people in their community, for fear that HCWs were infected with the SARS coronavirus (Bai et al., 2004; Koh et al., 2005). Even the families of HCWs were subject to such discrimination (Bai et al., 2004). Stigmatization adds an unnecessary burden to the lives of HCWs and can contribute to worker burnout (Lai et al., 2020; Ramaci, Barattucci, Ledda, & Rapisarda, 2020).

During the COVID-19 pandemic, HCWs have been widely praised as heroes in the popular media and by government leaders. Across the globe, it has become an evening ritual for people to publicly applaud HCWs. Does this mean that, unlike SARS, HCW stigmatization is not a problem during the COVID-19 pandemic? Cheering from the safety of one's balcony does not preclude the possibility of discriminatory attitudes toward HCWs, based on fears that these workers are carriers of SARSCoV2. To our knowledge, this issue has not been investigated in any systematic way.

The purpose of the present study was to investigate the prevalence and correlates of HCW stigmatization during the COVID-19 pandemic in a large sample of adults from the United States and Canada. We sought to assess the prevalence of stigma-related beliefs that HCWs are sources of infection with SARSCoV2, and identify the correlates of such attitudes, particularly the question of whether HCW-related stigmatizing attitudes are associated with the COVID Stress Syndrome. Recent research provides evidence of this syndrome (Taylor et al., 2020a, b). The core of the syndrome consists of (a) fears that COVID-19 is highly

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Table 1
Responses to the Healthcare Worker Stigmatization Survey (% endorsement).

	Strongly disagree	Disagree	Undecided	Agree	Strongly agree	Sum of agree or strongly agree
Healthcare workers who work in hospitals are likely to have COVID-19	6	26	36	26	6	32
For the safety of the community, healthcare workers should not go out in public	14	34	27	19	6	25
Healthcare workers should have some restrictions on their freedom	20	29	26	21	5	26
Healthcare workers who treat people with COVID-19 should be isolated	14	22	29	26	10	36
I do not want to be around healthcare workers who treat COVID-19 patients	11	19	24	33	14	47
I do not want to be around someone who works in a healthcare setting	15	28	25	24	9	33
Healthcare workers who treat people with COVID-19 should be separated from their families	17	21	32	23	8	31
I would not be comfortable visiting a healthcare worker for medical reasons because I would be worried I might get COVID-19	15	25	26	24	10	34

dangerous, combined with fears about coming into contact with fomites (surfaces or objects potentially contaminated with SARSCoV2), (b) fears about the personal socio-economic impact of COVID-19, and (c) xenophobic fears that foreigners are sources of infection. These fears are intercorrelated with one another and associated with COVID-related checking and reassurance-seeking, as well as COVID-related intrusive thoughts and nightmares (Taylor et al., 2020a, b).

Given that strongly-held fears about COVID-19 are at the core of the COVID Stress Syndrome, we expected that HCW-related stigmatizing attitudes (e.g., beliefs that HCWs are sources of COVID-19) would be strongly correlated with the COVID Stress Syndrome. If this is the case then it is also predicted that HCW-related stigmatizing attitudes, which involve fear and avoidance of HCWs, would be associated with other forms of avoidance during the COVID-19 pandemic, such as the avoidance of leaving the safety of one's home, avoidance of other people, and avoidance of essential stores such as supermarkets and drug stores because infected people might be at these stores.

We were further interested in the question of whether the nightly applauding of HCWs has any meaningful relationship to HCW stigma. Can stigmatization be reduced by encouraging people to applaud HCWs? If so, then the two should be negatively correlated. Alternatively, there might be no meaningful relationship between the two; people might applaud HCWs from the safety of their homes, while simultaneously fearing that HCWs are sources of infection and therefore having negative (e.g., shunning, avoidance) attitudes about HCWs.

2. Method

2.1. Sample and data collection procedures

Data were collected during May 6–19, 2020, from a random sample of adults from the United States and Canada. HCWs were excluded from the sample for the purpose of this study, resulting in 3551 non-HCW adults (1716 from the U.S., and 1835 from Canada). Data were collected using an internet-based self-report survey delivered in English by Qualtrics, a commercial survey sampling and administration company. All respondents provided written informed consent. Sample mean age was 54 years ($SD = 15$ years). A total of 42 % were female, most (92 %) were employed full- or part-time, and most (82 %) had completed full or partial college education. Most (69 %) were Caucasian, with the remainder being Asian (12 %), African American/Black (9%), Latino/Hispanic (6%), or other (4%). A total of 43 % reported having a pre-existing (i.e., pre-COVID-19) medical condition, and 16 % reported having a current (past year) mental health condition. Only 2% of the sample reported that they had been diagnosed with COVID-19.

2.2. Measures

Demographic and background variables were measured and coded as follows: Female sex (1 = yes, 0 = no), age (years), ethnic minority status (1 = yes, 0 = no), unemployed (1 = yes, 0 = no), full or partial college education (1 = yes, 0 = no), current (past year) mental health condition (1 = yes, 0 = no), pre-existing medical condition (1 = yes, 0 = no), and country (United States = 1, Canada = 0). Participants also completed the HCW Stigmatization Survey, which is an 8-item face-valid scale, developed for the purpose of the present study, measuring stigmatizing attitudes towards HCWs during COVID-19. The items, which are listed in Table 1, were rated on a 5-point scale (0=strongly disagree, 4=strongly agree). The items were unifactorial (as per Maximum Likelihood factor analysis plus parallel analysis), strongly correlated with one another (corrected item-total rs ranged from .48 to .78), and the reliability (internal consistency) was excellent; McDonald's $\omega = .93$. McDonald's ω was used instead of Cronbach's α because the former is a more accurate measure of reliability (McNeish, 2018). Values of ω are interpreted in the same way as α; that is, values in the range of .70–.80 indicate acceptable reliability, .80–.90 are good, and values greater than .90 are excellent.

COVID Stress Syndrome was assessed by the five COVID Stress Scales (see Table 3), which have very good reliability and validity (Taylor et al., 2020a). Avoidance of essential stores (i.e., supermarkets and drug stores) was assessed by two items, in which participants rated the extent of their avoidance of these stores during the past seven days on a 5-point scale (0=never, 4=almost always). Reliability of this scale was excellent ($\omega = .95$). The preference for avoiding people and for staying at home was assessed by two scales from the Hikikomori Questionnaire (Teo et al., 2018). Items for those scales were rated on a 5-point scale (0=strongly disagree, 4=strongly agree). Preference for avoiding people was assessed by an 8-item scale (e.g., "I prefer to stay away from other people"), and preference for remaining at home was measured by a 7-item scale (e.g., "I prefer to spend most of my time at home"). The reliabilities of these scales were acceptable-to-good; ωs were .88 and .79,

Table 2
Stigmatizing attitudes (% agree or strongly agree) for respondents who reported that they often or very often clapped or cheered for healthcare workers (n = 623).

	% agree or strongly agree
Healthcare workers who work in hospitals are likely to have COVID-19	39
For the safety of the community, healthcare workers should not go out in public	28
Healthcare workers should have some restrictions on their freedom	29
Healthcare workers who treat people with COVID-19 should be isolated	39
I do not want to be around healthcare workers who treat COVID-19 patients	42
I do not want to be around someone who works in a healthcare setting	30
Healthcare workers who treat people with COVID-19 should be separated from their families	35
I would not be comfortable visiting a healthcare worker for medical reasons because I would be worried I might get COVID-19	38

Table 3
Correlations with the total score on the Healthcare Worker Stigmatization Survey.

	r	p
Female sex	.12	<.001
Age	-.15	<.001
Minority status	.08	<.001
Unemployed	.03	.048
Completed full or partial college	-.03	.061
Pre-existing medical condition	-.03	.091
Current (past year) mental health condition	.05	<.001
Country (United States vs. Canada)	.00	.993
CSS: Fears about COVID-19 dangerousness and contamination	.45	<.001
CSS: Fears that foreigners are spreading COVID-19	.41	<.001
CSS: Fears about socio-economic effects of COVID-19	.32	<.001
CSS: COVID-related traumatic stress symptoms	.30	<.001
CSS: COVID-related compulsive checking and reassurance-seeking	.24	<.001
Avoidance of supermarkets and drug stores	.30	<.001
Preference for staying home	.31	<.001
Preference for avoiding people	.28	<.001

CSS = COVID Stress Scales. Classification of effect sizes: Yellow = small, pink = medium, red = large.

respectively. Applauding HCWs was assessed by asking respondents to rate their agreement with the following face valid statement: "In the past seven days, I have clapped and cheered for healthcare workers" (5-point rating, ranging from 0=never to 4=very often).

3. Results

Table 1 presents the descriptive statistics (% agreement) for the HCW Stigmatization Survey. More than a quarter of respondents believed that HCWs should have restrictions placed on their freedoms, such as not being allowed to go out in public, being isolated from the community, and being separated from their families. More than a third of respondents stated that they would avoid HCWs for fear of contracting COVID-19.

Table 4
Factor loadings for measures of stigma, avoidance, and COVID Stress Syndrome.

	Factor 1	Factor 2
CSS: Fears about COVID-19 dangerousness and contamination	**.81**	.07
CSS: Fears about socio-economic effects of COVID-19	**.80**	-.04
CSS: Fears that foreigners are spreading COVID-19	**.69**	-.06
CSS: COVID-related traumatic stress symptoms	**.68**	.03
CSS: COVID-related compulsive checking and reassurance-seeking	**.69**	-.13
Avoidance of supermarkets and drug stores	**.43**	.13
Healthcare Worker Stigmatization Survey	**.42**	.19
Preference for staying home	-.03	**.90**
Preference for avoiding people	.08	**.76**

CSS = COVID Stress Scales. Bold: Salient (≥.30) loading.

Participation in altruistic support of HCWs was unrelated to stigmatizing attitudes. The tendency to clap and cheer for HCWs during the evening applauding ritual had a near zero correlation ($r = .03$, $p = .08$) with the total score on the HCW Stigmatization Survey. Even for people who "often" or "very often" clapped and cheered for HCWs, many of these respondents feared and avoided HCWs. This is illustrated in Table 2, which presents the % agreement data of Table 1 but only for people who reported that they often or very often clapped and cheered for HCWs. Here, it can be seen that for people who applauded HCWs, more than a third believed that HCWs should have restrictions on their freedoms, be socially isolated, and separated from their families. More than a third of people who applauded HCWs stated that they would not want to be around HCWs, for fear of infection. Clearly, clapping and cheering for HCWs from the safety of one's home can occur in people who strongly fear, avoid, and stigmatize HCWs.

Table 3 presents the correlations (Pearson's r and, for dichotomous variables, biserial rs) between HCW stigmatization and demographic and other variables. Given the large sample size, substantively trivial correlations were statistically significant (e.g., for $r = .05$, $p < .001$). Accordingly, to facilitate the interpretation of correlations, we used Cohen (1988) criteria to classify correlations as small ($r = .10$), medium ($r = .30$), or large ($r = .50$). To give precision to these classifications for rs falling between the cutoffs, we classified r in terms of ranges, using the midpoints between .10 and .30, and between .30 and .50, so as to distinguish among small, medium, and large rs; that is, small .10-.19, medium .20-.39, and large >.39.

Table 3 shows that demographic and most other background variables had small or trivial correlations with HCW stigmatization. Stigmatization was more strongly correlated with the COVID Stress Scales and with measures of avoidance. People who stigmatized HCWs also tended to have features of the COVID Stress Syndrome (i.e., the five CSS variables in Table 3), to avoid other people, drug stores and supermarkets, and to avoid leaving their homes. The CSS was significantly correlated with the stigmatization scale, based on our community sample. This means that people with high scores on the CSS would tend to have higher levels of stigmatization than people randomly selected from the communities and countries that were sampled.

A Maximum Likelihood factor analysis of the COVID Stress Scales, avoidance measures, and HCW Stigmatization Survey yielded two correlated factors (as per parallel analysis; 51 % variance explained). Factors were correlated .37. Table 4 shows the factor loadings. Here, it can be seen that HCW stigmatization is linked to the COVID Stress Syndrome in that it loaded on the same factor as the COVID Stress Scales. Avoidance of people in general and the preference to stay at home formed a separate but correlated factor.

4. Discussion

Behind the facade of altruistic cheering and clapping for HCWs, there are important, under-recognized, and widespread stigmatizing attitudes toward healthcare providers. Our research suggests that many respondents in the community have grossly exaggerated estimates of the odds that HCWs are carriers of SARSCoV2. That is, almost a third (32 %) of respondents believed that HCWs are likely to have COVID-19 (Table 1). This stands in marked contrast to the research on COVID-19, which shows that the typical HCW is highly *unlikely* to be infected with SARSCoV2. American data (collected from February-April, 2020) shows that the majority of reported COVID-19 cases (89 %) were *not* HCWs (CDC COVID-19 Response Team, 2020). Canadian research shows that HCWs as a group (i.e., regardless of whether they specifically care for COVID-19 patients) have a risk of only 0.14 % of developing COVID-19, as compared to 0.10 % in the general population (COVID-19 Scientific Advisory Group, 2020). The higher prevalence was due, in part, to HCWs having a higher prevalence of testing for COVID-19 as compared to non-HCWs (15 % vs. 3%; COVID-19 Scientific Advisory Group, 2020). Among HCWs, the risk of being infected specifically as

part of their occupations was only .01 % (COVID-19 Scientific Advisory Group, 2020). This is consistent with research conducted in the Netherlands, which found that HCWs are more likely to acquire COVID-19 in the community, rather than in hospital settings (Kluytmans-van den Bergh et al., 2020). That is, just like non-HCWs, HCWs were most likely to be infected in the community rather than in hospital settings. Therefore, there is no sound basis for the attitudes of many of our participants, who believed that HCWs should be separated from their communities or families (see Table 1).

Globally, HCWs have a higher risk of acquiring COVID-19 as compared to non-HCWs (Koh, 2020), but even so, the majority (97 %) of HCWs have not been infected (COVID-19 Scientific Advisory Group, 2020). Although HCWs working with COVID-19 patients (e.g., in intensive care units) are at greater risk of exposure to SASCoV2, these workers are effectively protected by personal protective equipment (e.g., face masks, gloves, visors), which reduces the risk of infection to minimal levels (Liu et al., 2020). To illustrate, even among frontline HCWs in Wuhan, China (January-February, 2020), working in high-risk settings (i.e., clinics devoted to COVID-19), the incidence of COVID-19 was only 0.55 % (Lai et al., 2020). In other words, even in high risk settings, the overwhelming majority of HCWs (99.45 %) did not develop COVID-19. As observed by Cheng, Wong, and Yuen (2020), "this relatively low infection rate is reassuring, as it suggests that personal protect equipment, if available, can protect frontline HCWs directly caring for patients with COVID-19" (p. 1).

Although HCWs are at increased risk of infection with SARSCoV2 as compared to the general public, to our knowledge no health authority or government has recommended that HCWs be isolated from their communities or families during the COVID-19 pandemic. Indeed, such harsh measures would unnecessarily compound the stress already experienced by HCWs. Yet, our study revealed that a remarkably high percentage of Canadians and Americans expressed harsh attitudes about isolating HCWs, even to the point of believing that they should be denied access to their families.

How do these unrealistic attitudes arise? In some important ways, the COVID-19 pandemic had largely been a hidden pandemic, at least at the time of data collection (May 6–19, 2020). During the 1918 influenza pandemic, people were widely exposed to deaths in their communities, and the sight of coffins, hearses, and funerals were commonplace (Crosby, 2003). This has not been the case during the COVID-19 pandemic, where exposure to sickness and death has been, for the majority of people, a largely abstract experience in which fatalities are simply reported in the news media, rather than personally experienced. The majority of our respondents (84 %) did not even personally know anyone who had been diagnosed with COVID-19. HCW stigmatization was unrelated to whether the respondent personally knew anyone who had been infected by SARSCoV2 ($r = .02$, $p > .10$). Exposure to dramatic images of fatalities from the news media, along with dramatic news images of HCWs tending to the sick and dying, can cause the viewing public to overestimate the personal risk of infection (Taylor, 2019). In this context, many people in the present study held unrealistic attitudes about the dangers of coming into contact with HCWs.

The present study found evidence that the fear and avoidance of HCWs is part of a broader pattern of stigmatization. That is, people who tend to stigmatize (fear and avoid) HCWs also tend to stigmatize foreigners (i.e., are xenophobic, as assessed by the COVID Stress Scales) and also tend to avoid drug stores and pharmacies and, by extension, avoid retail workers in those stores. A question for further investigation concerns the breadth and boundaries of fear and avoidance. People with a high degree of fear and avoidance of HCWs may also tend to avoid other groups of people, for fear that the latter might be vectors of disease (e.g., children or sickly-looking people). Indeed, previous research concerning perceived vulnerability to disease suggests that people who are highly fearful of infection even stigmatize (e.g., avoid) people who only remotely have features suggestive of ill health (e.g., people who are old, disabled, or obese) (Schaller & Park, 2011). An issue for further research is whether HCW stigmatization is associated with stigmatization of people who have been infected with, and recovered from SARSCoV2. People who recovered from SARS were stigmatized (shunned, avoided) (Taylor, 2019) and there is concern that survivors of COVID-19 may be similarly stigmatized (World Health Organization, 2020). It remains to be determined whether this is part of a broader tendency to stigmatize people who are associated in some way with illness, and whether it is associated with the COVID Stress Syndrome.

Shunning, ostracism, and avoidance have been notable features of past pandemics and outbreaks, such as during the SARS outbreak (Taylor, 2019). Historians of pandemics have noted that survivors, public health officials, and political leaders tend to forget the lessons learned from previous pandemics (Crosby, 2003). The problem of pandemic-related stigmatization of HCWs is a lesson we have not learned. Cheering for HCWs is not enough. What is needed are clear, sensible, public education campaigns concerning the risks that HCWs pose to the public (see also Bhaumik, Moola, Tyagi, Nambiar, & Kakoti, 2020; Centers for Disease Control & Prevention, 2020).

The present study offers some clues about how to address the problem of HCW stigmatization. Correlational and factor analysis in this study indicates that the tendency to stigmatize HCWs is associated with the COVID Stress Syndrome. Previous research shows that the severity of this syndrome is correlated with the tendency to overestimate health risks in general (Taylor et al., 2020a, b). Thus, the fear and avoidance of HCWs is part of a broader tendency to overestimate health threats. Given that HCW stigmatization is linked to the COVID Stress Syndrome, it is possible that treating this syndrome might lead to a reduction in excessive fears of HCW, thereby reducing stigmatization. This could be done by means of cognitive-behavioral interventions or educational programs (Taylor & Asmundson, 2004; Taylor, 2019). Whether this is beneficial remains to be investigated in future research.

The present study has various strengths and limitations. In terms of strengths, the sample was large and, to our knowledge, this was the first systematic study to empirically investigate HCW stigmatization during COVID-19. In terms of limitations, the study was cross-sectional, conducted several months into the pandemic, and so it is possible that the attitudes and behaviors of respondents may change over time. Our assessment was limited to the self-report of attitudes and behaviors, rather than direct observational assessments of actual behaviors. Nevertheless, the findings are in keeping with studies conducted during the SARS outbreak (Bai et al., 2004; Koh et al., 2005). Further research into the largely unrecognized and under-appreciated issue of HCW stigmatization is needed to better understand and overcome this important societal problem.

There are many different avenues for further investigation. Future research is needed to evaluate the replicability and generalizability of the findings obtained in the present study. Research could be conducted to determine whether the findings are replicated using different methods to assess stigmatization. As part of this, alternative methods could be used to assess the respondents' estimations of the odds that HCWs are infected with SARSCoV2. Respondents could be asked, for example, to estimate the percentage of HCWs in their community that are currently infected with SARSCoV2, and this percentage could be compared with local prevalence statistics. The temporal stability of the tendency to stigmatize HCWs also needs to be investigated. Pandemics are dynamic events, in which psychological reactions change over time and circumstance (Taylor, 2019). The tendency to stigmatize HCWs could be trait-like or it might fluctuate, depending on whether the person feels personally threatened with infection. Alternatively, the tendency to stigmatize HCWs could have trait-like qualities (i.e., a baseline tendency to stigmatize) that are exacerbated and expressed when the person perceives that they are threatened with infection. Research on the perceived vulnerability to disease supports this combined trait and state conceptualization. That is, there is an enduring tendency (trait) for people to perceive themselves to be vulnerable to disease, and this vulnerability can be exacerbated when the person is exposed to health

threats, which has been shown to increase their tendency to stigmatize people who have superficial characteristics suggestive of poor health (e.g., the elderly, obese, or disabled) (Schaller & Park, 2011). Answers to these and related questions will help address the under-recognized and significant issue of pandemic-related HCW stigmatization.

Declaration of Competing Interest

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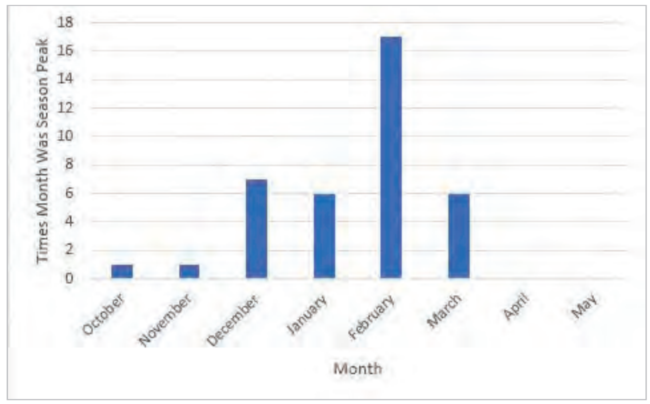
CDC Centers for Disease Control and Prevention

Flu Season

While seasonal influenza (flu) viruses are detected year-round in the United States, flu viruses are most common during the fall and winter. The exact timing and duration of flu seasons varies, but influenza activity often begins to increase in October. Most of the time flu activity peaks between December and February, although significant activity can last as late as May.

The figure below shows peak flu activity in the United States by month for the 1982-1983 through 2019-2020 flu seasons. The “peak month of flu activity” is the month with the highest percentage of respiratory specimens testing positive for influenza virus infection during that influenza season. During this 38-year period, flu activity most often peaked in February (17 seasons), followed by December (7 seasons), January (6 seasons) and March (6 seasons).

When is flu season in the United States?



In the United States, flu season occurs in the fall and winter. While influenza viruses spread year-round, most of the time flu activity peaks between December and February, but activity can last as late as May. The overall health impact (e.g., infections, hospitalizations, and deaths) of flu varies from season to season. CDC collects, compiles, and analyzes information on influenza activity year-round in the United States and produces FluView, a weekly surveillance report, and FluView Interactive, which allows for more in-depth exploration of influenza surveillance data. The Weekly U.S. Influenza Summary Update is updated weekly year-round.

How does CDC monitor the progress of flu season?

The overall health impact (e.g., infections, hospitalizations, and deaths) from flu varies from season to season. CDC collects, compiles, and analyzes information on influenza activity year-round in the United States and produces FluView, a weekly surveillance report, and FluView Interactive, which allows for more in-depth exploration of influenza surveillance data. The Weekly U.S. Influenza Summary Update is updated each week. The U.S. influenza surveillance system is a collaborative effort between CDC and its many partners in state and local health departments, public health and clinical laboratories, vital statistics offices, health care providers, and clinics and emergency departments. Information in five categories is collected from eight different data sources that allow CDC to:

- Find out when and where influenza activity is occurring
- Track influenza-related illness
- Determine what influenza viruses are circulating
- Detect changes in influenza viruses
- Measure the impact influenza is having on hospitalizations and deaths in the United States

These surveillance components allow CDC to determine when and where influenza activity is occurring, determine what types of influenza viruses are circulating, detect changes in the influenza viruses collected and analyzed, track patterns of influenza-related illness, and measure the impact of influenza in the United States. All influenza activity reporting by states, laboratories, and health care providers is voluntary. For more information about CDC’s influenza surveillance activities, see the Overview of Influenza Surveillance in the United States.

Why is there a week-long lag between when influenza surveillance data is collected and when it’s reported?

Influenza surveillance data collection is based on a reporting week that starts on Sunday and ends on the following Saturday of each week. Each surveillance participant is requested to summarize the weekly data and submit it to CDC by the following

Tuesday afternoon. The data are then downloaded, compiled, and analyzed at CDC. The data are used to update FluView and FluView Interactive on the following Friday.

Do other respiratory viruses circulate during flu season?

In addition to flu viruses, several other respiratory viruses also circulate during flu season and can cause symptoms similar to those seen with flu infection. These respiratory viruses include rhinovirus (one cause of the "common cold") and respiratory syncytial virus (RSV), which is the most common cause of severe respiratory illness in young children as well as a leading cause of death from respiratory illness in those aged 65 years and older.

Page last reviewed: September 28, 2021

France Covid: Vaccinations mandatory for all health workers

12 July

Coronavirus pandemic

From 21 July, people in France will need to show a 'health pass' to go to places like bars, cafes, shops and theatres

All health care workers in France must be fully vaccinated against Covid-19 by September or risk not being paid, the government has announced.

The requirement applies to doctors, nurses, office staff and volunteers.

President Emmanuel Macron has also said that from next month, health passes will need to be shown to access places like shops, bars and long-distance train journeys in France.

The passes show the holder has been jabbed, or had a recent negative test.

"I am aware of what I am asking of you, and I know that you are ready for this commitment, this is part, in a way, of your sense of duty," the president said in a televised address on Monday.

The mandatory vaccinations will apply to anyone who comes into contact with vulnerable people, and therefore applies to everyone who works in hospitals, clinics and care homes, regardless of their role.

They must be vaccinated by 15 September or risk not being paid, Health Minister Olivier Véran told France's LCI television.

Health passes are already used to enter some venues, such as nightclubs which reopened for the first time at the weekend. However they will be expanded to include more places including festivals, theatres and hospitals from 21 July and will apply to those aged over 12 years old.

To encourage people to get jabbed, PCR covid tests that are currently free will have to be paid for, unless accompanied with a doctor's prescription.

After the president's announcement, Doctolib, the website people use to book their jabs, crashed as so many people tried secure appointments.

- **France bans non-essential travel from UK**
- **Where is the Delta variant and how is it spreading?**

Cases are rising in France, with the Delta variant causing a surge in hospital admissions.

On Friday, a panel of scientists who advise the French government on health matters warned of a fourth wave in the coming months, and said as many as 95% of people may need to be vaccinated to control the spread.

However, only a little over half of the population has received a first dose and less than 40% have had two shots.

Ros Atkins On… Macron's Covid-19 Crisis

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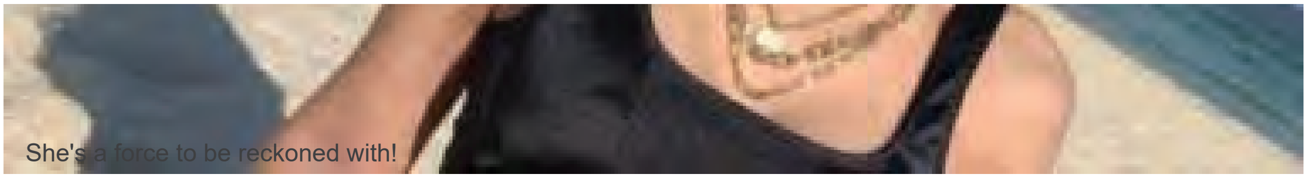

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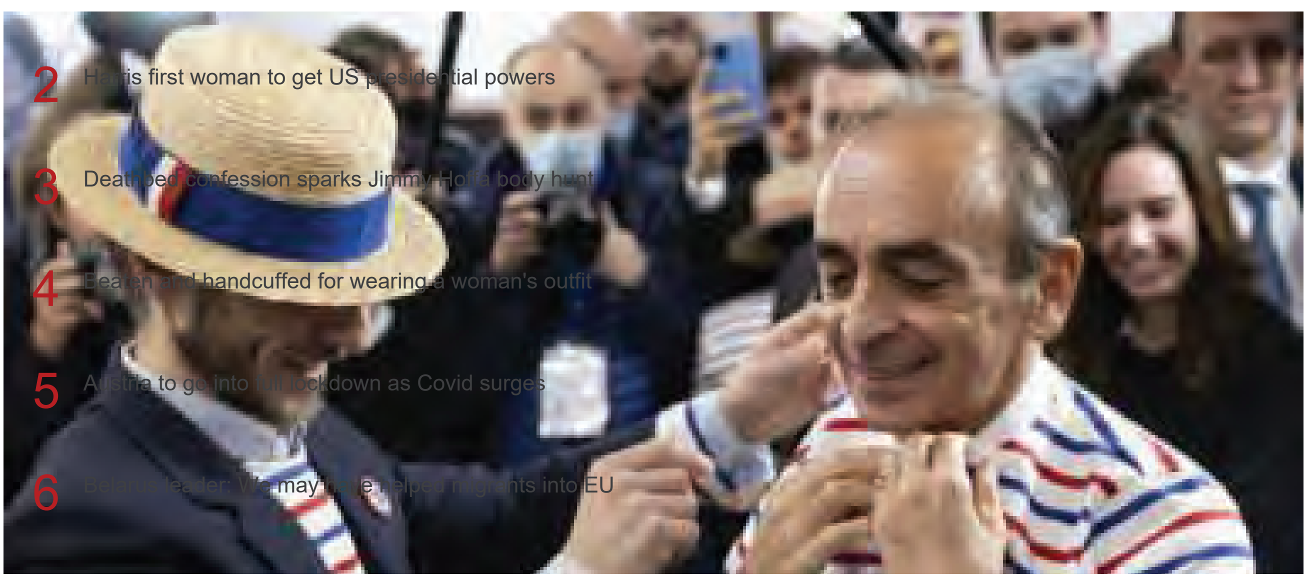

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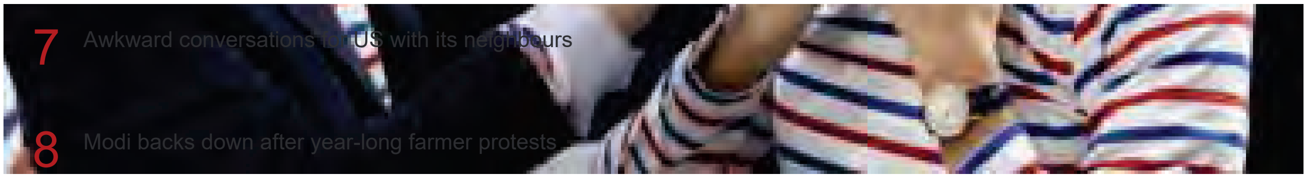

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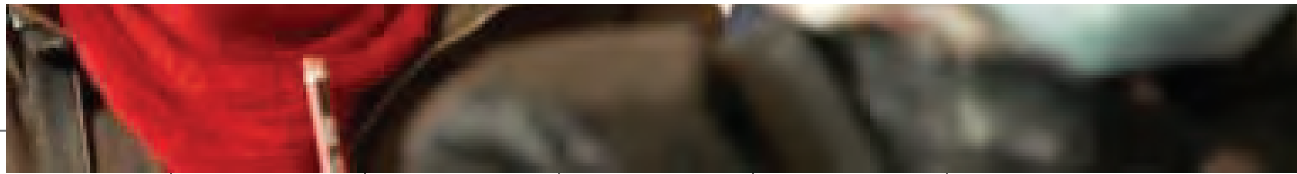

CDC Centers for Disease Control and Prevention

COVID-19

Frequently Asked Questions about COVID-19 Vaccination

Updated Nov. 4, 2021

NOTICE: CDC now recommends that children between the ages of 5 and 11 years receive the Pfizer-BioNTech pediatric COVID-19 Vaccine. Learn more about vaccines for children and teens.

- Below are answers to commonly asked questions about COVID-19 vaccination.
- Bust myths and learn the facts about COVID-19 vaccines

Safety

Are COVID-19 vaccines safe even though the vaccines were developed rapidly?

While COVID-19 vaccines were developed rapidly, all steps were taken to make sure they are safe and effective:

- **Approach to Development** – Scientists have been working for many years to develop vaccines against viruses like the one that causes COVID-19. This knowledge helped speed up the initial development of the current COVID-19 vaccines.
- **Clinical Trials** – All vaccines in the United States must go through three phases of clinical trials to make sure they are safe and effective. During the development of COVID-19 vaccines, phases overlapped to speed up the process, but all phases were completed.
- **Authorization or Approval** – Before vaccines are available to people, the U.S. Food and Drug Administration (FDA) assesses the findings from clinical trials. FDA determined that three COVID-19 vaccines met FDA's safety and effectiveness standards and granted those vaccines Emergency Use Authorizations (EUAs). This allowed the vaccines to be quickly distributed to control the pandemic. Pfizer-BioNTech (COMIRNATY) COVID-19 vaccine has now been FDA approved for people ages 16 years and older. Read more about the first COVID-19 vaccine to receive FDA approval.
- **Manufacturing and Distribution** – The U.S. government has invested substantial resources to manufacture and distribute COVID-19 vaccines. This allowed vaccine distribution to begin as soon as FDA authorized each vaccine.
- **Tracking Safety Using Vaccine Monitoring Systems –** COVID-19 vaccine safety monitoring has been the most intense and comprehensive in U.S. history. Hundreds of millions of people in the United States have received COVID-19 vaccines. Through several monitoring systems, CDC and FDA continue to provide updated information on the safety of these vaccines.

Learn more about developing COVID-19 vaccines.

What are the ingredients in COVID-19 vaccines?

vaccine ingredients vary by manufacturer. None of the vaccines contain eggs, gelatin, latex, or preservatives. All COVID-19 vaccines are **free from metals** such as iron, nickel, cobalt, lithium, and rare earth alloys. They are also free from manufactured products such as microelectronics, electrodes, carbon nanotubes, or nanowire semiconductors.

To learn more about the ingredients in authorized COVID-19 vaccines, see

- Pfizer-BioNTech COVID-19 Vaccine Overview and Safety
- Moderna COVID-19 Vaccine Overview and Safety
- Johnson & Johnson's Janssen COVID-19 Vaccine Overview and Safety
- Ingredients Included in COVID-19 Vaccines

If I am pregnant or planning to become pregnant, can I get a COVID-19 vaccine?

Yes, COVID-19 vaccination is recommended for all people 12 years and older, including people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future. You might want to have a conversation with your healthcare provider about COVID-19 vaccination. While such a conversation might be helpful, it is not required before vaccination. Learn more about vaccination considerations for people who are pregnant or breastfeeding.

If you are pregnant and have received a COVID-19 vaccine, we encourage you to enroll in **v-safe**, CDC's smartphone-based tool that provides personalized health check-ins after vaccination. A v-safe pregnancy registry has been established to gather information on the health of pregnant people who have received a COVID-19 vaccine.

Related pages:

- COVID-19 Vaccines for Pregnant or Breastfeeding People
- Monitoring Systems for Pregnant People
- V-safe Pregnancy Registry
- Planning for Pregnancy

Why should my child get vaccinated against COVID-19?

COVID-19 vaccination can help protect your child from getting COVID-19. Although fewer children have been sick with COVID-19 compared to adults, children can be infected with the virus that causes COVID-19, can get sick from COVID-19, and can spread the virus that causes COVID-19 to others. Getting your child vaccinated helps to protect your child and your family. Vaccination is now recommended for everyone 12 years and older. Currently, the Pfizer-BioNTech COVID-19 Vaccine is the only one available to children 12 years and older.

COVID-19 vaccines have been used under the most intensive safety monitoring in U.S. history, including studies in children 12 years and older. Your child cannot get COVID-19 from any COVID-19 vaccine. Like adults, children may have some side effects after COVID-19 vaccination. These side effects may affect their ability to do daily activities, but they should go away in a few days.

Related pages:

- COVID-19 Vaccines for Children and Teens
- Pfizer-BioNTech
- Possible Side Effects
- Families and Children

Getting Your Vaccine

Do I need a booster? How many doses of COVID-19 vaccine will I need to get?

COVID-19 Vaccine Primary Series

The number of vaccine doses you need depends on which vaccine you receive.

- Two doses of Pfizer-BioNTech vaccine should be given 3 weeks (21 days) apart.
- Two doses of Moderna vaccine should be given 4 weeks (28 days) apart.
- Only one dose of Johnson & Johnson's Janssen (J&J/Janssen) vaccine should be given.

If you receive a vaccine that requires two doses, you should get your second shot as close to the recommended interval as possible. You should **not** get the second dose earlier than the recommended interval.

COVID-19 vaccines **are not** interchangeable for your COVID-19 vaccine primary series.

If you received a Pfizer-BioNTech or Moderna COVID-19 vaccine for your first shot, you should get the same product for your second shot.

Additional Primary Dose If You Are Immunocompromised

If you received a Pfizer-BioNTech (ages 12 and older) or Moderna (ages 18 and older) mRNA COVID-19 vaccine primary series and have a moderately to severely compromised immune system, you should receive an additional primary dose of the same mRNA COVID-19 vaccine at least 28 days after the second dose.

Additional primary doses **are not** interchangeable. The additional mRNA COVID-19 dose should be the same vaccine product as the initial 2-dose mRNA COVID-19 vaccine primary series (Pfizer-BioNTech or Moderna). If the mRNA COVID-19 vaccine product given for the first two doses is not available, the other mRNA COVID-19 vaccine product may be used.

Currently, CDC does not recommend an **additional primary dose** if you received a single-dose J&J/Janssen COVID-19 vaccine or in children less than 12 years old with moderate or severely compromised immune systems.

Booster Shot

CDC recommends that if you received a primary series of an mRNA COVID-19 vaccine (i.e., Pfizer-BioNTech or Moderna) and are 65 years and older, 18 years and older and live in a long-term care setting, or are between the ages of 50 and 64 years and have certain underlying medical conditions, you **should** receive a single COVID-19 vaccine booster shot at least 6 months after you have completed your primary mRNA vaccine series.

CDC recommends everyone 18 years and older who received a J&J/Janssen COVID-19 vaccine primary dose **should** also receive a single COVID-19 vaccine booster shot at least 2 months after their primary dose.

If you are 18–64 years old and work or reside in high-risk settings, or if you are ages 18–49 years with certain underlying medical conditions, you **may** get a booster shot based on your individual risks and benefits.

Learn more about who is eligible for a COVID-19 vaccine booster shot.

If you get a booster shot you have the option to either get the same COVID-19 vaccine product as your primary series, or you can get a different COVID-19 vaccine. You may have a preference for the vaccine type that you originally received, and you may prefer to get a different booster. CDC's recommendations now allow for this type of mix and match dosing for booster shots (Pfizer-BioNTech, Moderna, or J&J/Janssen). You may consider the benefits and risks of each product and discuss with your healthcare provider which COVID-19 vaccine product is the most appropriate booster for you.

Currently, a booster shot is not recommended for children less than 18 years old.

If I didn't get my second shot of a 2-dose COVID-19 vaccine within the recommended time, what should I do?

You should **get your second shot as close to the recommended 3-week or 4-week interval as possible**. There is currently limited information on the effectiveness of receiving your second shot later than 6 weeks after the first shot. However, if you receive your second shot of COVID-19 vaccine at any time after the recommended date, you do not have to restart the vaccine series, and you can be considered fully vaccinated 2 weeks after getting your second shot. This guidance might be updated as more information becomes available.

Learn more about COVID-19 vaccines that require 2 shots.

How long does protection from a COVID-19 vaccine last?

It's not yet known how long COVID-19 vaccine protection lasts. Recent studies show that protection against the virus may decrease over time. This reduction in protection has led CDC to recommend certain groups of people get a booster shot. Some people who received Pfizer Vaccine or Moderna Vaccine should get a booster shot at least 6 months after completing their initial vaccination series. Anyone 18 years and older who received a J&J/Janssen Vaccine should get booster shot at least 2 months after their vaccine.

Learn more about who is eligible for a COVID-19 vaccine booster shot.

Related pages:

- Vaccines Work
- Booster Shots
- Moderately to Severely Immunocompromised People

Preparing for Your Vaccine

How long do I need to wait after getting a flu vaccine or another vaccine before getting a COVID-19 vaccine?

You can get a COVID-19 vaccine and other vaccines, including a flu vaccine, at the same visit. Experience with other vaccines has shown that the way our bodies develop protection, known as an immune response, and possible side effects after getting vaccinated are generally the same when given alone or with other vaccines. Learn more about the timing of other vaccines.

If I have already had COVID-19 and recovered, do I still need to get vaccinated with a COVID-19 vaccine?

Yes, you should be vaccinated regardless of whether you already had COVID-19 because:

- Research has not yet shown how long you are protected from getting COVID-19 again after you recover from COVID-19.
- Vaccination helps protect you even if you've already had COVID-19.

Evidence is emerging that people **get better protection by being fully vaccinated** compared with having had COVID-19. One study showed that unvaccinated people who already had COVID-19 are more than 2 times as likely than fully vaccinated people to get COVID-19 again.

If you were treated for COVID-19 with monoclonal antibodies or convalescent plasma, you should wait 90 days before getting a COVID-19 vaccine. Talk to your doctor if you are unsure what treatments you received or if you have more questions about getting a COVID-19 vaccine.

If you or your child has a history of multisystem inflammatory syndrome in adults or children (MIS-A or MIS-C), consider delaying vaccination until you or your child have recovered from being sick and for 90 days after the date of diagnosis of MIS-A or MIS-C. Learn more about the clinical considerations for people with a history of multisystem MIS-C or MIS-A.

Experts are still learning more about how long vaccines protect against COVID-19. CDC will keep the public informed as new evidence becomes available.

Related pages:

Can I get vaccinated against COVID-19 while I am currently sick with COVID-19?

No. People with COVID-19 who have symptoms should wait to be vaccinated until they have recovered from their illness and have met the criteria for discontinuing isolation; those without symptoms should also wait until they meet the criteria before getting vaccinated. This guidance also applies to people who get COVID-19 before getting their second dose of vaccine.

People who have had a known COVID-19 exposure should not seek vaccination until their quarantine period has ended to avoid potentially exposing healthcare personnel and others during the vaccination visit. This recommendation also applies to people with a known COVID-19 exposure who have received their first dose of an mRNA vaccine but not their second.

Related pages:

- When to Quarantine
- Ending Home Isolation

Can I choose which COVID-19 vaccine I get?

Yes. All currently authorized and recommended COVID-19 vaccines are safe and effective, and CDC does not recommend one vaccine over another. The most important decision is to get a COVID-19 vaccination as soon as possible. Widespread vaccination is a critical tool to help stop the pandemic.

People should be aware that a risk of a rare condition called thrombosis with thrombocytopenia syndrome (TTS) has been reported following vaccination with the J&J/Janssen COVID-19 Vaccine. TTS is a serious condition that involves blood clots with low platelet counts. This problem is rare, and most reports were in women between 18 and 49 years old. For women 50 years and older and men of any age, this problem is even more rare. There are other COVID-19 vaccine options available for which this risk has not been seen (Pfizer-BioNTech, Moderna).

Learn more about your COVID-19 vaccination, including how to find a vaccination location, what to expect at your appointment, and more.

Related page:

- Your Vaccination
- Safety of COVID-19 Vaccines

- Ensuring COVID-19 Vaccines Work

After Your Vaccine

How can I get a new COVID-19 vaccination card?

If you need a new vaccination card, contact the vaccination provider site where you received your vaccine. Your provider should give you a new card with up-to-date information about the vaccinations you have received.

If the location where you received your COVID-19 vaccine is no longer operating, contact your state or local health department's immunization information system (IIS) for assistance.

CDC does **not** maintain vaccination records or determine how vaccination records are used, and CDC does **not** provide the CDC-labeled, white COVID-19 vaccination record card to people. These cards are distributed to vaccination providers by state and local health departments. Please contact your state or local health department if you have additional questions about vaccination cards or vaccination records.

Related page:

- Getting Your CDC COVID-19 Vaccination Record Card

Do I need to wear a mask and avoid close contact with others if I am fully vaccinated?

After you are fully vaccinated for COVID-19, take these steps to protect yourself and others:

- In general, you do not need to wear a mask in outdoor settings.
- If you are in an area with high numbers of COVID-19 cases, consider wearing a mask in crowded outdoor settings and when you are in close contact with others who are not fully vaccinated.
- If you have a condition or taking medications that weaken your immune system, you may not be fully protected even if you are fully vaccinated. You should continue to take all precautions recommended for unvaccinated people, including wearing a well-fitted mask, until advised otherwise by their healthcare provider.
- If you are fully vaccinated, to maximize protection from the Delta variant and prevent possibly spreading it to others, wear a mask indoors in public if you are in an area of substantial or high transmission.

I was fully vaccinated in another country. How do I transfer my proof of vaccination from that country to get a proof of vaccination card in the United States?

CDC does **not** keep vaccination records or determine how vaccination records are used. To update your records with vaccines you received while outside of the United States, you may:

- Contact the immunization information system (IIS) in your state. You can find state IIS information on the CDC website.
- Contact your healthcare provider or your local or state immunization program through your state's health department.

The CDC-labeled white COVID-19 Vaccination Record Cards are only issued to people vaccinated in the United States. CDC recommends you keep your documentation of being vaccinated in the other country as proof of vaccination. CDC also recommends checking with your primary care provider or state health department for options to document your vaccination status domestically.

Am I considered fully vaccinated if I was vaccinated in another country?

You are considered fully vaccinated if you

- Received any single-dose COVID-19 vaccine series that is authorized or approved by the U.S. Food and Drug Administration (FDA) or listed for emergency use by World Health Organization (WHO).
- *Received any combination of two doses of an FDA approved/authorized or WHO emergency use listed COVID-19 two-dose series with at least 17 days between doses.

**CDC does not recommend mixing different COVID-19 vaccines for the primary series, but CDC is aware that this is increasingly common in many countries outside of the United States. Therefore, for the interpretation of vaccination records, these people are considered fully vaccinated.*

The WHO emergency use list currently includes the following vaccines:

- **Pfizer-BioNTech COVID-19 Vaccine**– FDA-authorized, (labeled as COMIRNATY in European Union), 2 doses, for adolescents 12 -15 years old
- **Pfizer-BioNTech (COMIRNATY) COVID-19 Vaccine**– FDA-approved, 2 doses, for persons 16 years and older
- **Moderna COVID-19 Vaccine**– FDA-authorized, 2 doses, for persons 18 years and older
- **Johnson and Johnson's Janssen COVID-19 Vaccine**– FDA-authorized, (labeled as Janssen-Cilag in European Union), 1 dose, for persons 18 years and older
- **AstraZeneca COVID-19 Vaccine**– WHO-listed, (labeled as COVISHIELD in Canada and others, labeled as AstraZeneca/SKBio in Republic of Korea), 2 doses, for persons 18 years and older
- **Sinopharm BIBP COVID-19 Vaccine**– WHO-listed, 2 doses, for persons 18 years and older
- **Sinovac-CoronaVac COVID-19 Vaccine**– WHO-listed, 2 doses, for persons 18 years and older

If you received a COVID-19 vaccine that is **not** authorized or approved by FDA or listed for emergency use by WHO, you may start over with an FDA-authorized or approved COVID-19 vaccine. Please note that no data are available on the safety or effectiveness of COVID-19 vaccination after receiving a non-FDA-authorized or approved COVID-19 vaccine. Wait at least 28 days after you received the last dose of the non-FDA-authorized or approved vaccine before receiving an FDA-authorized or approved COVID-19 vaccine.

Visit the clinical considerations webpage for more information.

Answers to more questions about:

- Healthcare Professionals and COVID-19 Vaccines
- Vaccines.gov
- Vaccine Administration Management System (VAMS)
- V-safe after Vaccination Health Checker

Last Updated Nov. 4, 2021

Frequently Asked Questions About Therapeutic Biological Products

These frequently asked questions have been developed for the CDER Small Business and Industry Assistance Web site (/cder-small-business-and-industry-assistance) to help small pharmaceutical businesses understand the regulatory process for therapeutic biological products.

1. **What is a biological product?**

   Biological products, like other drugs, are used for the treatment, prevention or cure of disease in humans. In contrast to chemically synthesized small molecular weight drugs, which have a well-defined structure and can be thoroughly characterized, biological products are generally derived from living material--human, animal, or microorganism--are complex in structure, and thus are usually not fully characterized.

   Section 351 of the *Public Health Service (PHS) Act* defines a biological product as a "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, ... applicable to the prevention, treatment, or cure of a disease or condition of human beings." FDA regulations and policies have established that biological products include blood-derived products, vaccines, in vivo diagnostic allergenic products, immunoglobulin products, products containing cells or microorganisms, and most protein products. Biological products subject to the *PHS Act* also meet the definition of *drugs* under the *Federal Food, Drug and Cosmetic Act (FDC Act)*. Note that hormones such as insulin, glucagon, and human growth hormone are regulated as drugs under the *FDC Act*, not biological products under the *PHS Act*.

2. **What Center has the regulatory responsibility for therapeutic biological products?**

   Both the FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) have regulatory responsibility for therapeutic biological products, including premarket review and oversight. The categories of therapeutic biological products regulated by CDER (under the *FDC Act* and/or the *PHS Act*, as appropriate) are the following

   - Monoclonal antibodies for in vivo use.
   - Most proteins intended for therapeutic use, including cytokines (e.g., interferons), enzymes (e.g. thrombolytics), and other novel proteins, except for those that are specifically assigned to the Center for Biologics Evaluation and Research (CBER) (e.g., vaccines and blood products). This category includes therapeutic proteins

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derived from plants, animals, humans, or microorganisms, and recombinant versions of these products. Exceptions to this rule are coagulation factors (both recombinant and human-plasma derived).

- Immunomodulators (non-vaccine and non-allergenic products intended to treat disease by inhibiting or down-regulating a pre-existing, pathological immune response).
- Growth factors, cytokines, and monoclonal antibodies intended to mobilize, stimulate, decrease or otherwise alter the production of hematopoietic cells in vivo.

Please refer to the Transfer of Therapeutic Biological Products to the Center for Drug Evaluation and Research (/about-fda/about-center-biologics-evaluation-and-research/transfer-therapeutic-products-center-drug-evaluation-and-research-cder) for updates that further define the categories of biological products that are regulated by CDER and CBER.

3. **Are the biologic development requirements different than the requirements for a new drug product?**

Biological products are a subset of drugs; therefore both are regulated under provisions of the FDC Act. However, only biological products are licensed under section 351 of the PHS Act. (As previously noted, some therapeutic protein products are approved under section 505 of the FDC Act, not under the PHS Act.)

Following initial laboratory and animal testing that show that investigational use in humans is reasonably safe, biological products (like other drugs), can be studied in clinical trials in humans under an investigational new drug application (IND) in accordance with the regulations at 21 CFR 312. If the data generated by the studies demonstrate that the product is safe and effective for its intended use, the data are submitted as part of a marketing application. Whereas a new drug application (NDA) is used for drugs subject to the drug approval provisions of the FDC Act, a biologics license application (BLA) is required for biological products subject to licensure under the PHS Act. FDA form 356h is used for both NDA and BLA submissions. FDA approval to market a biologic is granted by issuance of a biologics license.

4. **What are the requirements for licensing a biologic?**

Issuance of a biologics license is a determination that the product, the manufacturing process, and the manufacturing facilities meet applicable requirements to ensure the continued safety, purity and potency of the product.

Among other things, safety and purity assessments must consider the storage and testing of cell substrates that are often used to manufacture biologics. A potency assay is required due to the complexity and heterogeneity of biologics.

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The regulations regarding BLAs for therapeutic biological products include *21 CFR parts 600 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=600&showFR=1), 601 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=601&showFR=1), and 610 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=610&showFR=1)*.

5. **What does safety mean?**

   The word safety means the relative freedom from harmful effects, direct or indirect, when a product is prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time.

6. **What is purity?**

   Purity means relative freedom from extraneous matter in the finished product, whether or not harmful to the recipient or deleterious to the product. Purity includes but is not limited to relative freedom from residual moisture or other volatile substances and pyrogenic substances.

7. **What is potency?**

   The word potency is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests, to yield a given result.

8. **Does FDA issue license certificates upon approval of a BLA?**

   Approval to market a biologic is granted by issuance of a biologics license (including US license number) as part of the approval letter. FDA does not issue a license certificate. The US License number must appear on the product labeling.

9. **Why are biologics regulated under the *PHS Act*?**

   As mentioned above, biologics are subject to provisions of both the *FD&C Act* and the *PHS Act*. Because of the complexity of manufacturing and characterizing a biologic, the *PHS Act* emphasizes the importance of appropriate manufacturing control for products. The *PHS Act* provides for a system of controls over all aspects of the manufacturing process. In some cases, manufacturing changes could result in changes to the biological molecule that might not be detected by standard chemical and molecular biology characterization techniques yet could profoundly alter the safety or efficacy profile. Therefore, changes in the manufacturing process, equipment or facilities may require additional clinical studies to demonstrate the product's continued safety, identity, purity and potency.

   The *PHS Act* also provides authority to immediately suspend licenses in situations where there exists a danger to public health.

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10. **10. How is the manufacturing process for a biological product usually different from the process for drugs?**

    Because, in many cases, there is limited ability to identify the identity of the clinically active component(s) of a complex biological product, such products are often defined by their manufacturing processes. Changes in the manufacturing process, equipment or facilities could result in changes in the biological product itself and sometimes require additional clinical studies to demonstrate the product's safety, identity, purity and potency. Traditional drug products usually consist of pure chemical substances that are easily analyzed after manufacture. Since there is a significant difference in how biological products are made, the production is monitored by the agency from the early stages to make sure the final product turns out as expected.

11. **What is comparability testing of biologics?**

    A sponsor may be able to demonstrate product comparability between a biological product made after a manufacturing change and a product made before implementation of the change through different types of analytical and functional testing without additional clinical studies. The agency may determine that the two products are comparable if the results of the comparability testing demonstrate that the manufacturing change does not affect safety, identity, purity, or potency. For more information see *FDA Guidance Concerning Demonstration of Comparability of Human Biological Products including Therapeutic Biotechnology-derived Products* (/drugs/guidances-drugs/demonstration-comparability-human-biological-products-including-therapeutic-biotechnology-derived).

Additional Information

12. **Where can I find additional information about therapeutic biologics?**

    There are several guidances that may be helpful.

    - "Changes to an Approved Application for Specified Biotechnology and Specified Synthetic Biological Products" (PDF - 33KB) (/media/75318/download)
    - "Content and Format of INDs for Phase I Studies of Drugs Including Well-Characterized, Therapeutic, Biotechnology-derived products" (PDF - 42KB) (/media/71203/download)
    - "Providing Clinical Effectiveness of Human Drugs and Biological Products (/biologics-guidances)"
    - "Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use" (PDF - 140KB) (/media/76798/download)

13. **Who should I contact if I still have questions about therapeutic biologics?**

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You should contact the Regulatory Project Manager (RPM) in the Office of New Drugs review division that is assigned responsibility for your application. As with all drugs regulated by CDER, applications are reviewed by a multidisciplinary review team. For biologics, the Chemistry, Manufacturing, and Controls (CMC) information is reviewed by staff in the Office of Biotechnology Products and manufacturing facility-related information is reviewed by the Therapeutics Facilities Review Branch in the Office of Compliance.

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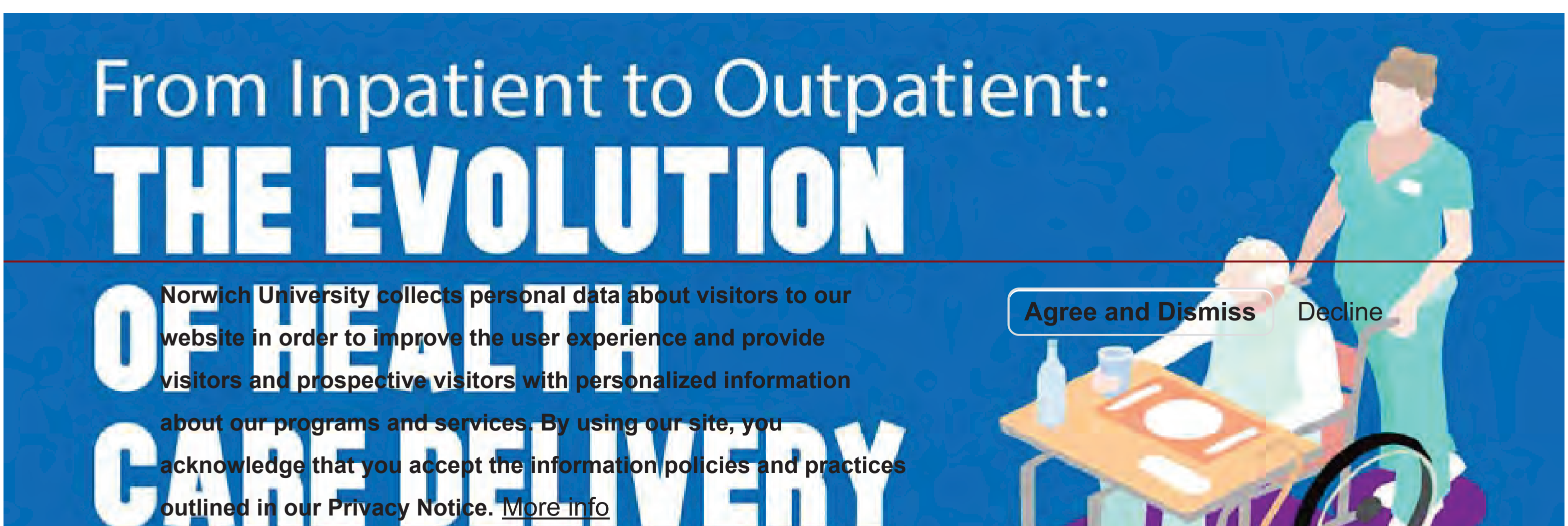
Infographic

From Inpatient to Outpatient: The Evolution of Healthcare Delivery

Nursing: Leadership & Education
by Norwich University Online | September 12th, 2018

The healthcare industry has been making efforts to improve the efficiency and affordability of services. Lots of changes have occurred in the past few years as a result of this drive. There has been a decrease in hospital admissions as more people are served through outpatient care. Nurses are also being given new opportunities to work with patients and their communities. To learn more, check out this infographic.

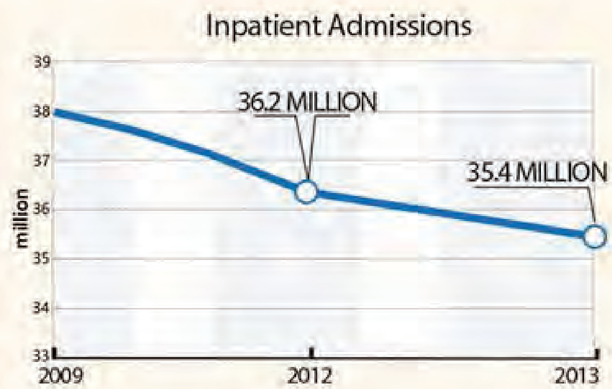


Efforts to improve health care efficiency and lower costs have resulted in a change in where health care is being delivered. Fewer patients are being admitted to hospitals, and there are new opportunities for nurses to provide care for patients and their communities.

TRENDS IN HEALTH CARE DELIVERY

According to the American Hospital Association, there has been a decline in hospital admissions since 2009

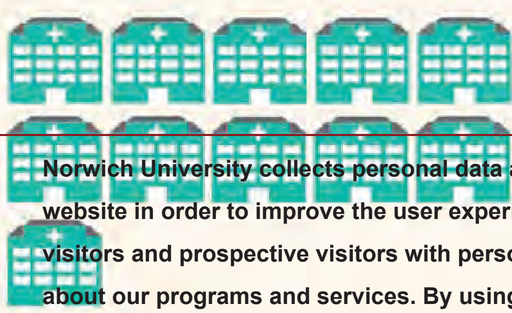
In 2013, there was a **2%** decline in hospital inpatient admissions to approximately 35.4 million, compared with almost 36.2 million admissions reported in 2012



787 MILLION Outpatient visits, however, increased 1.2% to more than 787 million in 2013

From 2006 to 2013, the number of outpatient observation stays increased by 96%

According to a 2015 report by the **Medicare Payment Advisory Commission** (MedPAC), over the past seven years, the use of outpatient services has increased 33%



The **Cleveland Clinic Health System** reported that inpatient admissions for the 11-hospital network fell **3.25%** to 38,880 for the quarter ended September 30, 2014, down from 40,186 during the same period one year ago.

Outpatient observation admissions at the health system increased 14.15% during

the same three months in 2014.

The 2014 Construction & Design Survey by Modern Healthcare indicated that the majority of hospital construction has shifted away from inpatient-based projects and toward outpatient-based projects, such as building or renovating medical office buildings, urgent care centers, or emergency departments.

GOALS AND EXPECTATIONS OF ALTERNATIVE DELIVERY SYSTEMS

Many hospitals, health systems and payers are adopting **health care delivery system** reforms with the goal of better aligning provider incentives to:

- **Improve the patient experience** (including quality and satisfaction of care)
- **Improve the health of populations**
- **Reduce the per capita cost of healthcare**

The **Affordable Care Act** established a new framework to move the U.S. health care system away from rewarding health providers for the quantity of care they provide and toward rewarding quality.

TYPES OF OUTPATIENT FACILITIES

NURSE MANAGED HEALTH CENTERS (NMHCs)

NMHCs are health care delivery sites operated by Advanced Practice Registered Nurses (APRNs)

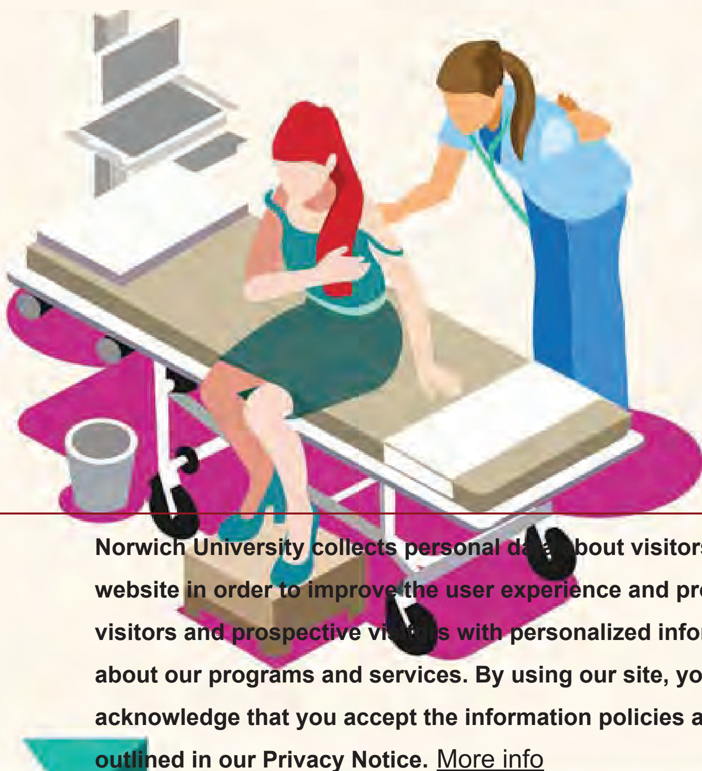
NMHCs provide primary care, with a focus on health promotion and disease prevention to individuals with limited access to care, regardless of their ability to pay

Services available at these clinics include physical exams, cardiovascular checks, diabetes and osteoporosis screenings, smoking cessation programs, immunizations, and other prevention-focused services.

There are at least **200** NMHCs currently operating in 37 states with an estimated 2 million patient encounters per year

AMBULATORY CARE NURSING

Ambulatory care nurses care for patients in environments outside of the hospital, focusing on general health education



SETTINGS INCLUDE

- **Hospital-based clinics/centers**
- **Ambulatory surgery & diagnostic procedure centers**
- **Telehealth service environments**
- **Military and veterans administration settings**
- **Colleges and educational institutions**
- **Patient homes**

HOW TECHNOLOGY IS DRIVING THE EVOLUTION OF HEALTH CARE DELIVERY

While outpatient care has become more common due to several factors, new technologies have provided nurses with additional tools that can aid with patient care outside of acute care settings.

mHealth: Mobile health is freeing health care devices of wires and cords and enabling nurses and patients alike to check on health care processes on-the-go.

The number of mobile health applications available to consumers now surpasses 165,000.

Telemedicine/telehealth: Studies consistently show the benefit of telehealth, especially in rural settings that do not have access to the same resources metropolitan areas may have. Examples include, allowing patients to track blood pressure, blood oxygen levels, weight, etc. at home.

The Electronic Health Record (EHR): The EHR automates access to information and has the potential to streamline the clinician's workflow. The EHR also has the ability to support other care-related activities directly or indirectly through various interfaces, including evidence-based decision support, quality management, and outcomes reporting.

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NORWICH UNIVERSITY Online

ONLINE.NORWICH.EDU/NURSING

Text: Inpatient to Outpatient Evolution

Trends in Health Care Delivery

Studies of hospital admissions throughout the country reveal an ongoing decline which started in 2009. The changes have been small but steady. For instance, there were almost 36.2 million admissions in 2012 according to the American Hospital Association. By 2013, this fell to about 35.4 million which translates to a drop of 2%. The outpatient figures, meanwhile, show an opposite trend. This type of visit to the hospitals actually increased in the same time period to over 787 million for a rise of 1.2%. This might seem like a small percentage but the large base means that the number of people affected is nontrivial.

If we look at a broader time span, then the changes appear to be truly startling. The number of outpatient observation stays increased by 96% from 2006 to 2013. In other words, visits nearly doubled in a period of six years. A Medicare Payment Advisory Commission report released in 2015 supports these findings. This MedPac paper says that the use of outpatient services increased by 33% over the past seven years. Various events and activities are being suggested as the reason for this clear shift.

The Cleveland Clinic Health System also published its own study on the matter. They focused on the number of inpatient admissions for an 11-hospital network and found a 3.25% fall in 2014. They had 40,186 visits in 2013 which dropped to 38.880 the following year. The opposite happened on the outpatient side of things in the health system. They observed a 14.15% increase during the exact same period.

All of these changes have begun to have a tangible impact in the way that hospitals are planning to respond to patient needs. For instance, Modern Healthcare did a survey on hospital construction and design in 2014. They found that the majority of these institutions have shifted their funding in line with the trends. There is now more allocation for outpatient-based projects such as renovations of emergency departments and urgent care centers.

Goals and Expectations of Alternative Delivery Systems

A large block of the healthcare industry is responding to the changing environment by implementing much-needed reforms. Incentives are now being aligned to encourage improvement certain aspects of delivery. The primary objective is to enhance the patient experience which includes increasing the quality of care, thereby getting better satisfaction rates. They are also concerned with the development of the health of the population as a whole. They look at the community and not just the individual patients. Finally, they would like to reduce the per capita cost of healthcare. The Affordable Care Act is crucial in providing a framework for rewarding providers according to the quality of their service.

Types of Outpatient Facilities

Nurse Managed Health Centers are sites which are operated by Advanced Practice Registered Nurses. These NMHCs provide primary care to patients while focusing on the promotion of good health habits and disease prevention. They typically cater to individuals who have limited access to care regardless of their ability to pay. These clinics offer a wide variety of service including physical exams, diabetes screenings, cardiovascular checks, smoking cessation programs, osteoporosis screenings, immunizations, and the like. As of the last count, there are about 200 NMHCs scattered across 37 states. They get about two million patient encounters every year.

Ambulatory care nursing is provided in multiple settings. The nurses engaged in this type of service care for patients in environments outside of the hospitals. They have a firm focus on general health education. Ambulatory nurses are often found in telehealth service environments providing information to people who are miles away. They could be in military and veterans administration settings, colleges and educational institutions, ambulatory surgery centers, diagnostic procedure facilities, and even patient homes. They make routine visits to check on people and provide whatever assistance is required by the patients.

How Technology is Driving Evolution

Technology has had a major impact on virtually every industry including health care. Modes of delivery are changing rapidly. Nurses now have more tools that they can use to help them as they attend to patients outside of acute care settings. These include mHealth, telemedicine, and electronic health records.

mHealth brings the convenience and flexibility of mobile computing to the delivery of health services. Nurses can have all the information that they need anywhere they are so they are no longer tied to the monolithic system at the hospitals. Patients can use these as well to check on processes throughout the day. They don't even have to go to a healthcare facility to get the info they need or the help they require. The number of mHealth apps available to consumers is now more than 165,000. These range from heart rate monitors to medication reminders.

Telemedicine is the delivery of services over long distances with the aid of technology. This often happens real-time with doctors, nurses, and patients talking to each other onscreen via the Internet. Other arrangements are also possible depending on the facilities available. Studies in this area have routinely praised telemedicine for its role in providing healthcare to isolated regions. Rural towns, for example, often lack medical experts who can diagnose and treat the sick. This technology can help bridge the gap by giving them access to urban doctors at a very low cost. They don't have to travel far to get quality service.

Health records are increasingly becoming digitized for storage in massive databases. This makes retrieval much easier for everyone from patients to clinicians. Doctors can make better decisions regarding their patients thanks to the information that is always just a click away. Electronic health records also make care delivery more efficient as everything is streamlined. Aside from providing all the details on demand, the systems may also come with interfaces for outcomes reporting, quality management, and evidence-based decision support.

Learn More

Norwich University has been a leader in innovative education since 1819. Through its online programs, Norwich delivers relevant and applicable curricula that allow its students to make a positive impact on their places of work and their communities.

Norwich University's online Master of Science in Nursing (/nursing) program helps students hone their knowledge and skills to assume leadership positions in healthcare systems, nursing informatics or nursing education. The program aims to develop students who could take a role in shaping health policy, in educating other nurses and healthcare professionals, and in providing advanced care to their patients. Norwich's online nursing program coursework has been developed based on guidelines by the American Association of Colleges of Nursing, and the program is accredited by the Commission on Collegiate Nursing Education.

Explore this Program

Nursing: Leadership & Education (/academic-programs/masters/nursing/leadership-education-informatics)

Nursing: Nurse Practitioner (/academic-programs/masters/nursing/nurse-practitioner)

Find out more

Privacy Policy (/about-us/privacy-policy)
Student Consumer Information (http://www.norwich.edu/consumer)
Non-Discriminatory Statement (/about-us/non-discrimination-statement)
Use of Military Photography (/military/use-of-military-photos)

Public Law 110–233
110th Congress

An Act

To prohibit discrimination on the basis of genetic information with respect to health insurance and employment.

May 21, 2008
[H.R. 493]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Genetic Information Non-discrimination Act of 2008.
42 USC 2000ff note.

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Genetic Information Nondiscrimination Act of 2008".

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

SEC. 2. FINDINGS.

42 USC 2000ff note.

Congress makes the following findings:

(1) Deciphering the sequence of the human genome and other advances in genetics open major new opportunities for medical progress. New knowledge about the genetic basis of illness will allow for earlier detection of illnesses, often before symptoms have begun. Genetic testing can allow individuals to take steps to reduce the likelihood that they will contract

a particular disorder. New knowledge about genetics may allow for the development of better therapies that are more effective against disease or have fewer side effects than current treatments. These advances give rise to the potential misuse of genetic information to discriminate in health insurance and employment.

(2) The early science of genetics became the basis of State laws that provided for the sterilization of persons having presumed genetic "defects" such as mental retardation, mental disease, epilepsy, blindness, and hearing loss, among other conditions. The first sterilization law was enacted in the State of Indiana in 1907. By 1981, a majority of States adopted sterilization laws to "correct" apparent genetic traits or tendencies. Many of these State laws have since been repealed, and many have been modified to include essential constitutional requirements of due process and equal protection. However, the current explosion in the science of genetics, and the history of sterilization laws by the States based on early genetic science, compels Congressional action in this area.

(3) Although genes are facially neutral markers, many genetic conditions and disorders are associated with particular racial and ethnic groups and gender. Because some genetic traits are most prevalent in particular groups, members of a particular group may be stigmatized or discriminated against as a result of that genetic information. This form of discrimination was evident in the 1970s, which saw the advent of programs to screen and identify carriers of sickle cell anemia, a disease which afflicts African-Americans. Once again, State legislatures began to enact discriminatory laws in the area, and in the early 1970s began mandating genetic screening of all African Americans for sickle cell anemia, leading to discrimination and unnecessary fear. To alleviate some of this stigma, Congress in 1972 passed the National Sickle Cell Anemia Control Act, which withholds Federal funding from States unless sickle cell testing is voluntary.

(4) Congress has been informed of examples of genetic discrimination in the workplace. These include the use of pre-employment genetic screening at Lawrence Berkeley Laboratory, which led to a court decision in favor of the employees in that case Norman-Bloodsaw v. Lawrence Berkeley Laboratory (135 F.3d 1260, 1269 (9th Cir. 1998)). Congress clearly has a compelling public interest in relieving the fear of discrimination and in prohibiting its actual practice in employment and health insurance.

(5) Federal law addressing genetic discrimination in health insurance and employment is incomplete in both the scope and depth of its protections. Moreover, while many States have enacted some type of genetic non-discrimination law, these laws vary widely with respect to their approach, application, and level of protection. Congress has collected substantial evidence that the American public and the medical community find the existing patchwork of State and Federal laws to be confusing and inadequate to protect them from discrimination. Therefore Federal legislation establishing a national and uniform basic standard is necessary to fully protect the public from discrimination and allay their concerns about the potential

for discrimination, thereby allowing individuals to take advantage of genetic testing, technologies, research, and new therapies.

TITLE I—GENETIC NONDISCRIMINATION IN HEALTH INSURANCE

SEC. 101. AMENDMENTS TO EMPLOYEE RETIREMENT INCOME SECURITY ACT OF 1974.

(a) NO DISCRIMINATION IN GROUP PREMIUMS BASED ON GENETIC INFORMATION.—Section 702(b) of the Employee Retirement Income Security Act of 1974 (29 U.S.C. 1182(b)) is amended—

(1) in paragraph (2)(A), by inserting before the semicolon the following: "except as provided in paragraph (3)"; and

(2) by adding at the end the following:

"(3) NO GROUP-BASED DISCRIMINATION ON BASIS OF GENETIC INFORMATION.—

"(A) IN GENERAL.—For purposes of this section, a group health plan, and a health insurance issuer offering group health insurance coverage in connection with a group health plan, may not adjust premium or contribution amounts for the group covered under such plan on the basis of genetic information.

"(B) RULE OF CONSTRUCTION.—Nothing in subparagraph (A) or in paragraphs (1) and (2) of subsection (d) shall be construed to limit the ability of a health insurance issuer offering health insurance coverage in connection with a group health plan to increase the premium for an employer based on the manifestation of a disease or disorder of an individual who is enrolled in the plan. In such case, the manifestation of a disease or disorder in one individual cannot also be used as genetic information about other group members and to further increase the premium for the employer.".

(b) LIMITATIONS ON GENETIC TESTING; PROHIBITION ON COLLECTION OF GENETIC INFORMATION; APPLICATION TO ALL PLANS.—Section 702 of the Employee Retirement Income Security Act of 1974 (29 U.S.C. 1182) is amended by adding at the end the following:

"(c) GENETIC TESTING.—

"(1) LIMITATION ON REQUESTING OR REQUIRING GENETIC TESTING.—A group health plan, and a health insurance issuer offering health insurance coverage in connection with a group health plan, shall not request or require an individual or a family member of such individual to undergo a genetic test.

"(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to limit the authority of a health care professional who is providing health care services to an individual to request that such individual undergo a genetic test.

"(3) RULE OF CONSTRUCTION REGARDING PAYMENT.—

"(A) IN GENERAL.—Nothing in paragraph (1) shall be construed to preclude a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, from obtaining and using the results of a genetic test in making a determination regarding payment (as such term is defined for the purposes of applying the regulations promulgated by the

Secretary of Health and Human Services under part C of title XI of the Social Security Act and section 264 of the Health Insurance Portability and Accountability Act of 1996, as may be revised from time to time) consistent with subsection (a).

"(B) LIMITATION.—For purposes of subparagraph (A), a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, may request only the minimum amount of information necessary to accomplish the intended purpose.

"(4) RESEARCH EXCEPTION.—Notwithstanding paragraph (1), a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, may request, but not require, that a participant or beneficiary undergo a genetic test if each of the following conditions is met:

"(A) The request is made, in writing, pursuant to research that complies with part 46 of title 45, Code of Federal Regulations, or equivalent Federal regulations, and any applicable State or local law or regulations for the protection of human subjects in research.

"(B) The plan or issuer clearly indicates to each participant or beneficiary, or in the case of a minor child, to the legal guardian of such beneficiary, to whom the request is made that—

"(i) compliance with the request is voluntary; and

"(ii) non-compliance will have no effect on enrollment status or premium or contribution amounts.

"(C) No genetic information collected or acquired under this paragraph shall be used for underwriting purposes.

Notification.

"(D) The plan or issuer notifies the Secretary in writing that the plan or issuer is conducting activities pursuant to the exception provided for under this paragraph, including a description of the activities conducted.

"(E) The plan or issuer complies with such other conditions as the Secretary may by regulation require for activities conducted under this paragraph.

"(d) PROHIBITION ON COLLECTION OF GENETIC INFORMATION.—

"(1) IN GENERAL.—A group health plan, and a health insurance issuer offering health insurance coverage in connection with a group health plan, shall not request, require, or purchase genetic information for underwriting purposes (as defined in section 733).

"(2) PROHIBITION ON COLLECTION OF GENETIC INFORMATION PRIOR TO ENROLLMENT.—A group health plan, and a health insurance issuer offering health insurance coverage in connection with a group health plan, shall not request, require, or purchase genetic information with respect to any individual prior to such individual's enrollment under the plan or coverage in connection with such enrollment.

"(3) INCIDENTAL COLLECTION.—If a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, obtains genetic information incidental to the requesting, requiring, or purchasing of other information concerning any individual, such request, requirement, or purchase shall not be considered a violation

of paragraph (2) if such request, requirement, or purchase is not in violation of paragraph (1).

"(e) APPLICATION TO ALL PLANS.—The provisions of subsections (a)(1)(F), (b)(3), (c), and (d), and subsection (b)(1) and section 701 with respect to genetic information, shall apply to group health plans and health insurance issuers without regard to section 732(a).".

(c) APPLICATION TO GENETIC INFORMATION OF A FETUS OR EMBRYO.—Such section is further amended by adding at the end the following:

"(f) GENETIC INFORMATION OF A FETUS OR EMBRYO.—Any reference in this part to genetic information concerning an individual or family member of an individual shall—

"(1) with respect to such an individual or family member of an individual who is a pregnant woman, include genetic information of any fetus carried by such pregnant woman; and

"(2) with respect to an individual or family member utilizing an assisted reproductive technology, include genetic information of any embryo legally held by the individual or family member.".

(d) DEFINITIONS.—Section 733(d) of the Employee Retirement Income Security Act of 1974 (29 U.S.C. 1191b(d)) is amended by adding at the end the following:

"(5) FAMILY MEMBER.—The term 'family member' means, with respect to an individual—

"(A) a dependent (as such term is used for purposes of section 701(f)(2)) of such individual, and

"(B) any other individual who is a first-degree, second-degree, third-degree, or fourth-degree relative of such individual or of an individual described in subparagraph (A).

"(6) GENETIC INFORMATION.—

"(A) IN GENERAL.—The term 'genetic information' means, with respect to any individual, information about—

"(i) such individual's genetic tests,

"(ii) the genetic tests of family members of such individual, and

"(iii) the manifestation of a disease or disorder in family members of such individual.

"(B) INCLUSION OF GENETIC SERVICES AND PARTICIPATION IN GENETIC RESEARCH.—Such term includes, with respect to any individual, any request for, or receipt of, genetic services, or participation in clinical research which includes genetic services, by such individual or any family member of such individual.

"(C) EXCLUSIONS.—The term 'genetic information' shall not include information about the sex or age of any individual.

"(7) GENETIC TEST.—

"(A) IN GENERAL.—The term 'genetic test' means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.

"(B) EXCEPTIONS.—The term 'genetic test' does not mean—

"(i) an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes; or

"(ii) an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

"(8) GENETIC SERVICES.—The term 'genetic services' means—

"(A) a genetic test;

"(B) genetic counseling (including obtaining, interpreting, or assessing genetic information); or

"(C) genetic education.

"(9) UNDERWRITING PURPOSES.—The term 'underwriting purposes' means, with respect to any group health plan, or health insurance coverage offered in connection with a group health plan—

"(A) rules for, or determination of, eligibility (including enrollment and continued eligibility) for benefits under the plan or coverage;

"(B) the computation of premium or contribution amounts under the plan or coverage;

"(C) the application of any pre-existing condition exclusion under the plan or coverage; and

"(D) other activities related to the creation, renewal, or replacement of a contract of health insurance or health benefits.".

(e) ERISA ENFORCEMENT.—Section 502 of the Employee Retirement Income Security Act of 1974 (29 U.S.C. 1132) is amended—

(1) in subsection (a)(6), by striking "(7), or (8)" and inserting "(7), (8), or (9)";

(2) in subsection (b)(3), by striking "The Secretary" and inserting "Except as provided in subsections (c)(9) and (a)(6) (with respect to collecting civil penalties under subsection (c)(9)), the Secretary"; and

(3) in subsection (c), by redesignating paragraph (9) as paragraph (10), and by inserting after paragraph (8) the following new paragraph:

"(9) SECRETARIAL ENFORCEMENT AUTHORITY RELATING TO USE OF GENETIC INFORMATION.—

"(A) GENERAL RULE.—The Secretary may impose a penalty against any plan sponsor of a group health plan, or any health insurance issuer offering health insurance coverage in connection with the plan, for any failure by such sponsor or issuer to meet the requirements of subsection (a)(1)(F), (b)(3), (c), or (d) of section 702 or section 701 or 702(b)(1) with respect to genetic information, in connection with the plan.

"(B) AMOUNT.—

"(i) IN GENERAL.—The amount of the penalty imposed by subparagraph (A) shall be $100 for each day in the noncompliance period with respect to each participant or beneficiary to whom such failure relates.

"(ii) NONCOMPLIANCE PERIOD.—For purposes of this paragraph, the term 'noncompliance period' means, with respect to any failure, the period—

"(I) beginning on the date such failure first occurs; and

"(II) ending on the date the failure is corrected.

"(C) MINIMUM PENALTIES WHERE FAILURE DISCOVERED.—Notwithstanding clauses (i) and (ii) of subparagraph (D):

"(i) IN GENERAL.—In the case of 1 or more failures with respect to a participant or beneficiary—

"(I) which are not corrected before the date on which the plan receives a notice from the Secretary of such violation; and

"(II) which occurred or continued during the period involved;

the amount of penalty imposed by subparagraph (A) by reason of such failures with respect to such participant or beneficiary shall not be less than $2,500.

"(ii) HIGHER MINIMUM PENALTY WHERE VIOLATIONS ARE MORE THAN DE MINIMIS.—To the extent violations for which any person is liable under this paragraph for any year are more than de minimis, clause (i) shall be applied by substituting '$15,000' for '$2,500' with respect to such person.

"(D) LIMITATIONS.—

"(i) PENALTY NOT TO APPLY WHERE FAILURE NOT DISCOVERED EXERCISING REASONABLE DILIGENCE.—No penalty shall be imposed by subparagraph (A) on any failure during any period for which it is established to the satisfaction of the Secretary that the person otherwise liable for such penalty did not know, and exercising reasonable diligence would not have known, that such failure existed.

"(ii) PENALTY NOT TO APPLY TO FAILURES CORRECTED WITHIN CERTAIN PERIODS.—No penalty shall be imposed by subparagraph (A) on any failure if—

"(I) such failure was due to reasonable cause and not to willful neglect; and

"(II) such failure is corrected during the 30-day period beginning on the first date the person otherwise liable for such penalty knew, or exercising reasonable diligence would have known, that such failure existed.

"(iii) OVERALL LIMITATION FOR UNINTENTIONAL FAILURES.—In the case of failures which are due to reasonable cause and not to willful neglect, the penalty imposed by subparagraph (A) for failures shall not exceed the amount equal to the lesser of—

"(I) 10 percent of the aggregate amount paid or incurred by the plan sponsor (or predecessor plan sponsor) during the preceding taxable year for group health plans; or

"(II) $500,000.

"(E) WAIVER BY SECRETARY.—In the case of a failure which is due to reasonable cause and not to willful neglect, the Secretary may waive part or all of the penalty imposed by subparagraph (A) to the extent that the payment of such penalty would be excessive relative to the failure involved.

"(F) DEFINITIONS.—Terms used in this paragraph which are defined in section 733 shall have the meanings provided such terms in such section.".

29 USC 1132 note.

(f) REGULATIONS AND EFFECTIVE DATE.—

(1) REGULATIONS.—The Secretary of Labor shall issue final regulations not later than 12 months after the date of enactment of this Act to carry out the amendments made by this section.

Applicability.

(2) EFFECTIVE DATE.—The amendments made by this section shall apply with respect to group health plans for plan years beginning after the date that is 1 year after the date of enactment of this Act.

SEC. 102. AMENDMENTS TO THE PUBLIC HEALTH SERVICE ACT.

(a) AMENDMENTS RELATING TO THE GROUP MARKET.—

(1) NO DISCRIMINATION IN GROUP PREMIUMS BASED ON GENETIC INFORMATION.—Section 2702(b) of the Public Health Service Act (42 U.S.C. 300gg–1(b)) is amended—

(A) in paragraph (2)(A), by inserting before the semicolon the following: "except as provided in paragraph (3)"; and

(B) by adding at the end the following:

"(3) NO GROUP-BASED DISCRIMINATION ON BASIS OF GENETIC INFORMATION.—

"(A) IN GENERAL.—For purposes of this section, a group health plan, and health insurance issuer offering group health insurance coverage in connection with a group health plan, may not adjust premium or contribution amounts for the group covered under such plan on the basis of genetic information.

"(B) RULE OF CONSTRUCTION.—Nothing in subparagraph (A) or in paragraphs (1) and (2) of subsection (d) shall be construed to limit the ability of a health insurance issuer offering health insurance coverage in connection with a group health plan to increase the premium for an employer based on the manifestation of a disease or disorder of an individual who is enrolled in the plan. In such case, the manifestation of a disease or disorder in one individual cannot also be used as genetic information about other group members and to further increase the premium for the employer.".

(2) LIMITATIONS ON GENETIC TESTING; PROHIBITION ON COLLECTION OF GENETIC INFORMATION; APPLICATION TO ALL PLANS.—Section 2702 of the Public Health Service Act (42 U.S.C. 300gg–1) is amended by adding at the end the following:

"(c) GENETIC TESTING.—

"(1) LIMITATION ON REQUESTING OR REQUIRING GENETIC TESTING.—A group health plan, and a health insurance issuer offering health insurance coverage in connection with a group health plan, shall not request or require an individual or a family member of such individual to undergo a genetic test.

"(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to limit the authority of a health care professional who is providing health care services to an individual to request that such individual undergo a genetic test.

"(3) RULE OF CONSTRUCTION REGARDING PAYMENT.—

"(A) IN GENERAL.—Nothing in paragraph (1) shall be construed to preclude a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, from obtaining and using the results of a genetic test in making a determination regarding payment (as such term is defined for the purposes of applying the regulations promulgated by the Secretary under part C of title XI of the Social Security Act and section 264 of the Health Insurance Portability and Accountability Act of 1996, as may be revised from time to time) consistent with subsection (a).

"(B) LIMITATION.—For purposes of subparagraph (A), a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, may request only the minimum amount of information necessary to accomplish the intended purpose.

"(4) RESEARCH EXCEPTION.—Notwithstanding paragraph (1), a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, may request, but not require, that a participant or beneficiary undergo a genetic test if each of the following conditions is met:

"(A) The request is made pursuant to research that complies with part 46 of title 45, Code of Federal Regulations, or equivalent Federal regulations, and any applicable State or local law or regulations for the protection of human subjects in research.

"(B) The plan or issuer clearly indicates to each participant or beneficiary, or in the case of a minor child, to the legal guardian of such beneficiary, to whom the request is made that—

"(i) compliance with the request is voluntary; and

"(ii) non-compliance will have no effect on enrollment status or premium or contribution amounts.

"(C) No genetic information collected or acquired under this paragraph shall be used for underwriting purposes.

"(D) The plan or issuer notifies the Secretary in writing that the plan or issuer is conducting activities pursuant to the exception provided for under this paragraph, including a description of the activities conducted. Notification.

"(E) The plan or issuer complies with such other conditions as the Secretary may by regulation require for activities conducted under this paragraph.

"(d) PROHIBITION ON COLLECTION OF GENETIC INFORMATION.—

"(1) IN GENERAL.—A group health plan, and a health insurance issuer offering health insurance coverage in connection with a group health plan, shall not request, require, or purchase genetic information for underwriting purposes (as defined in section 2791).

"(2) PROHIBITION ON COLLECTION OF GENETIC INFORMATION PRIOR TO ENROLLMENT.—A group health plan, and a health insurance issuer offering health insurance coverage in connection with a group health plan, shall not request, require, or purchase genetic information with respect to any individual prior to such individual's enrollment under the plan or coverage in connection with such enrollment.

"(3) INCIDENTAL COLLECTION.—If a group health plan, or a health insurance issuer offering health insurance coverage in connection with a group health plan, obtains genetic information incidental to the requesting, requiring, or purchasing of other information concerning any individual, such request, requirement, or purchase shall not be considered a violation of paragraph (2) if such request, requirement, or purchase is not in violation of paragraph (1).

"(e) APPLICATION TO ALL PLANS.—The provisions of subsections (a)(1)(F), (b)(3), (c) , and (d) and subsection (b)(1) and section 2701 with respect to genetic information, shall apply to group health plans and health insurance issuers without regard to section 2721(a).".

(3) APPLICATION TO GENETIC INFORMATION OF A FETUS OR EMBRYO.—Such section is further amended by adding at the end the following:

"(f) GENETIC INFORMATION OF A FETUS OR EMBRYO.—Any reference in this part to genetic information concerning an individual or family member of an individual shall—

"(1) with respect to such an individual or family member of an individual who is a pregnant woman, include genetic information of any fetus carried by such pregnant woman; and

"(2) with respect to an individual or family member utilizing an assisted reproductive technology, include genetic information of any embryo legally held by the individual or family member.".

(4) DEFINITIONS.—Section 2791(d) of the Public Health Service Act (42 U.S.C. 300gg–91(d)) is amended by adding at the end the following:

"(15) FAMILY MEMBER.—The term 'family member' means, with respect to any individual—

"(A) a dependent (as such term is used for purposes of section 2701(f)(2)) of such individual; and

"(B) any other individual who is a first-degree, second-degree, third-degree, or fourth-degree relative of such individual or of an individual described in subparagraph (A).

"(16) GENETIC INFORMATION.—

"(A) IN GENERAL.—The term 'genetic information' means, with respect to any individual, information about—

"(i) such individual's genetic tests,

"(ii) the genetic tests of family members of such individual, and

"(iii) the manifestation of a disease or disorder in family members of such individual.

"(B) INCLUSION OF GENETIC SERVICES AND PARTICIPATION IN GENETIC RESEARCH.—Such term includes, with respect to any individual, any request for, or receipt of, genetic services, or participation in clinical research which includes genetic services, by such individual or any family member of such individual.

"(C) EXCLUSIONS.—The term 'genetic information' shall not include information about the sex or age of any individual.

"(17) GENETIC TEST.—

"(A) IN GENERAL.—The term 'genetic test' means an analysis of human DNA, RNA, chromosomes, proteins, or

metabolites, that detects genotypes, mutations, or chromosomal changes.

"(B) EXCEPTIONS.—The term 'genetic test' does not mean—

"(i) an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes; or

"(ii) an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

"(18) GENETIC SERVICES.—The term 'genetic services' means—

"(A) a genetic test;

"(B) genetic counseling (including obtaining, interpreting, or assessing genetic information); or

"(C) genetic education.

"(19) UNDERWRITING PURPOSES.—The term 'underwriting purposes' means, with respect to any group health plan, or health insurance coverage offered in connection with a group health plan—

"(A) rules for, or determination of, eligibility (including enrollment and continued eligibility) for benefits under the plan or coverage;

"(B) the computation of premium or contribution amounts under the plan or coverage;

"(C) the application of any pre-existing condition exclusion under the plan or coverage; and

"(D) other activities related to the creation, renewal, or replacement of a contract of health insurance or health benefits.".

(5) REMEDIES AND ENFORCEMENT.—Section 2722(b) of the Public Health Service Act (42 U.S.C. 300gg–22(b)) is amended by adding at the end the following:

"(3) ENFORCEMENT AUTHORITY RELATING TO GENETIC DISCRIMINATION.—

"(A) GENERAL RULE.—In the cases described in paragraph (1), notwithstanding the provisions of paragraph (2)(C), the succeeding subparagraphs of this paragraph shall apply with respect to an action under this subsection by the Secretary with respect to any failure of a health insurance issuer in connection with a group health plan, to meet the requirements of subsection (a)(1)(F), (b)(3), (c), or (d) of section 2702 or section 2701 or 2702(b)(1) with respect to genetic information in connection with the plan.

"(B) AMOUNT.—

"(i) IN GENERAL.—The amount of the penalty imposed under this paragraph shall be $100 for each day in the noncompliance period with respect to each participant or beneficiary to whom such failure relates. Penalties.

"(ii) NONCOMPLIANCE PERIOD.—For purposes of this paragraph, the term 'noncompliance period' means, with respect to any failure, the period—

"(I) beginning on the date such failure first occurs; and

"(II) ending on the date the failure is corrected.

"(C) MINIMUM PENALTIES WHERE FAILURE DISCOVERED.—Notwithstanding clauses (i) and (ii) of subparagraph (D):

"(i) IN GENERAL.—In the case of 1 or more failures with respect to an individual—

"(I) which are not corrected before the date on which the plan receives a notice from the Secretary of such violation; and

"(II) which occurred or continued during the period involved;

the amount of penalty imposed by subparagraph (A) by reason of such failures with respect to such individual shall not be less than $2,500.

"(ii) HIGHER MINIMUM PENALTY WHERE VIOLATIONS ARE MORE THAN DE MINIMIS.—To the extent violations for which any person is liable under this paragraph for any year are more than de minimis, clause (i) shall be applied by substituting '$15,000' for '$2,500' with respect to such person.

"(D) LIMITATIONS.—

"(i) PENALTY NOT TO APPLY WHERE FAILURE NOT DISCOVERED EXERCISING REASONABLE DILIGENCE.—No penalty shall be imposed by subparagraph (A) on any failure during any period for which it is established to the satisfaction of the Secretary that the person otherwise liable for such penalty did not know, and exercising reasonable diligence would not have known, that such failure existed.

"(ii) PENALTY NOT TO APPLY TO FAILURES CORRECTED WITHIN CERTAIN PERIODS.—No penalty shall be imposed by subparagraph (A) on any failure if—

"(I) such failure was due to reasonable cause and not to willful neglect; and

"(II) such failure is corrected during the 30-day period beginning on the first date the person otherwise liable for such penalty knew, or exercising reasonable diligence would have known, that such failure existed.

"(iii) OVERALL LIMITATION FOR UNINTENTIONAL FAILURES.—In the case of failures which are due to reasonable cause and not to willful neglect, the penalty imposed by subparagraph (A) for failures shall not exceed the amount equal to the lesser of—

"(I) 10 percent of the aggregate amount paid or incurred by the employer (or predecessor employer) during the preceding taxable year for group health plans; or

"(II) $500,000.

"(E) WAIVER BY SECRETARY.—In the case of a failure which is due to reasonable cause and not to willful neglect, the Secretary may waive part or all of the penalty imposed by subparagraph (A) to the extent that the payment of such penalty would be excessive relative to the failure involved.".

(b) AMENDMENT RELATING TO THE INDIVIDUAL MARKET.—

(1) IN GENERAL.—The first subpart 3 of part B of title XXVII of the Public Health Service Act (42 U.S.C. 300gg–51 et seq.) (relating to other requirements) is amended—

(A) by redesignating such subpart as subpart 2; and

(B) by adding at the end the following:

"SEC. 2753. PROHIBITION OF HEALTH DISCRIMINATION ON THE BASIS OF GENETIC INFORMATION.

42 USC 300gg–53.

"(a) PROHIBITION ON GENETIC INFORMATION AS A CONDITION OF ELIGIBILITY.—

"(1) IN GENERAL.—A health insurance issuer offering health insurance coverage in the individual market may not establish rules for the eligibility (including continued eligibility) of any individual to enroll in individual health insurance coverage based on genetic information.

"(2) RULE OF CONSTRUCTION.—Nothing in paragraph (1) or in paragraphs (1) and (2) of subsection (e) shall be construed to preclude a health insurance issuer from establishing rules for eligibility for an individual to enroll in individual health insurance coverage based on the manifestation of a disease or disorder in that individual, or in a family member of such individual where such family member is covered under the policy that covers such individual.

"(b) PROHIBITION ON GENETIC INFORMATION IN SETTING PREMIUM RATES.—

"(1) IN GENERAL.—A health insurance issuer offering health insurance coverage in the individual market shall not adjust premium or contribution amounts for an individual on the basis of genetic information concerning the individual or a family member of the individual.

"(2) RULE OF CONSTRUCTION.—Nothing in paragraph (1) or in paragraphs (1) and (2) of subsection (e) shall be construed to preclude a health insurance issuer from adjusting premium or contribution amounts for an individual on the basis of a manifestation of a disease or disorder in that individual, or in a family member of such individual where such family member is covered under the policy that covers such individual. In such case, the manifestation of a disease or disorder in one individual cannot also be used as genetic information about other individuals covered under the policy issued to such individual and to further increase premiums or contribution amounts.

"(c) PROHIBITION ON GENETIC INFORMATION AS PREEXISTING CONDITION.—

"(1) IN GENERAL.—A health insurance issuer offering health insurance coverage in the individual market may not, on the basis of genetic information, impose any preexisting condition exclusion (as defined in section 2701(b)(1)(A)) with respect to such coverage.

"(2) RULE OF CONSTRUCTION.—Nothing in paragraph (1) or in paragraphs (1) and (2) of subsection (e) shall be construed to preclude a health insurance issuer from imposing any preexisting condition exclusion for an individual with respect to health insurance coverage on the basis of a manifestation of a disease or disorder in that individual.

"(d) GENETIC TESTING.—

"(1) LIMITATION ON REQUESTING OR REQUIRING GENETIC TESTING.—A health insurance issuer offering health insurance coverage in the individual market shall not request or require an individual or a family member of such individual to undergo a genetic test.

"(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to limit the authority of a health care professional who is providing health care services to an individual to request that such individual undergo a genetic test.

"(3) RULE OF CONSTRUCTION REGARDING PAYMENT.—

"(A) IN GENERAL.—Nothing in paragraph (1) shall be construed to preclude a health insurance issuer offering health insurance coverage in the individual market from obtaining and using the results of a genetic test in making a determination regarding payment (as such term is defined for the purposes of applying the regulations promulgated by the Secretary under part C of title XI of the Social Security Act and section 264 of the Health Insurance Portability and Accountability Act of 1996, as may be revised from time to time) consistent with subsection (a) and (c).

"(B) LIMITATION.—For purposes of subparagraph (A), a health insurance issuer offering health insurance coverage in the individual market may request only the minimum amount of information necessary to accomplish the intended purpose.

"(4) RESEARCH EXCEPTION.—Notwithstanding paragraph (1), a health insurance issuer offering health insurance coverage in the individual market may request, but not require, that an individual or a family member of such individual undergo a genetic test if each of the following conditions is met:

"(A) The request is made pursuant to research that complies with part 46 of title 45, Code of Federal Regulations, or equivalent Federal regulations, and any applicable State or local law or regulations for the protection of human subjects in research.

"(B) The issuer clearly indicates to each individual, or in the case of a minor child, to the legal guardian of such child, to whom the request is made that—

"(i) compliance with the request is voluntary; and

"(ii) non-compliance will have no effect on enrollment status or premium or contribution amounts.

"(C) No genetic information collected or acquired under this paragraph shall be used for underwriting purposes.

Notification.

"(D) The issuer notifies the Secretary in writing that the issuer is conducting activities pursuant to the exception provided for under this paragraph, including a description of the activities conducted.

"(E) The issuer complies with such other conditions as the Secretary may by regulation require for activities conducted under this paragraph.

"(e) PROHIBITION ON COLLECTION OF GENETIC INFORMATION.—

"(1) IN GENERAL.—A health insurance issuer offering health insurance coverage in the individual market shall not request, require, or purchase genetic information for underwriting purposes (as defined in section 2791).

"(2) PROHIBITION ON COLLECTION OF GENETIC INFORMATION PRIOR TO ENROLLMENT.—A health insurance issuer offering

health insurance coverage in the individual market shall not request, require, or purchase genetic information with respect to any individual prior to such individual's enrollment under the plan in connection with such enrollment.

"(3) INCIDENTAL COLLECTION.—If a health insurance issuer offering health insurance coverage in the individual market obtains genetic information incidental to the requesting, requiring, or purchasing of other information concerning any individual, such request, requirement, or purchase shall not be considered a violation of paragraph (2) if such request, requirement, or purchase is not in violation of paragraph (1).

"(f) GENETIC INFORMATION OF A FETUS OR EMBRYO.—Any reference in this part to genetic information concerning an individual or family member of an individual shall—

"(1) with respect to such an individual or family member of an individual who is a pregnant woman, include genetic information of any fetus carried by such pregnant woman; and

"(2) with respect to an individual or family member utilizing an assisted reproductive technology, include genetic information of any embryo legally held by the individual or family member.".

(2) REMEDIES AND ENFORCEMENT.—Section 2761(b) of the Public Health Service Act (42 U.S.C. 300gg–61(b)) is amended to read as follows:

"(b) SECRETARIAL ENFORCEMENT AUTHORITY.—The Secretary shall have the same authority in relation to enforcement of the provisions of this part with respect to issuers of health insurance coverage in the individual market in a State as the Secretary has under section 2722(b)(2), and section 2722(b)(3) with respect to violations of genetic nondiscrimination provisions, in relation to the enforcement of the provisions of part A with respect to issuers of health insurance coverage in the small group market in the State.".

(c) ELIMINATION OF OPTION OF NON-FEDERAL GOVERNMENTAL PLANS TO BE EXCEPTED FROM REQUIREMENTS CONCERNING GENETIC INFORMATION.—Section 2721(b)(2) of the Public Health Service Act (42 U.S.C. 300gg–21(b)(2)) is amended—

(1) in subparagraph (A), by striking "If the plan sponsor" and inserting "Except as provided in subparagraph (D), if the plan sponsor"; and

(2) by adding at the end the following:

"(D) ELECTION NOT APPLICABLE TO REQUIREMENTS CONCERNING GENETIC INFORMATION.—The election described in subparagraph (A) shall not be available with respect to the provisions of subsections (a)(1)(F), (b)(3), (c), and (d) of section 2702 and the provisions of sections 2701 and 2702(b) to the extent that such provisions apply to genetic information.".

(d) REGULATIONS AND EFFECTIVE DATE.— 42 USC 300gg–1 note.

(1) REGULATIONS.—Not later than 12 months after the date of enactment of this Act, the Secretary of Health and Human Services shall issue final regulations to carry out the amendments made by this section.

(2) EFFECTIVE DATE.—The amendments made by this section shall apply— Applicability.

(A) with respect to group health plans, and health insurance coverage offered in connection with group health plans, for plan years beginning after the date that is 1 year after the date of enactment of this Act; and

(B) with respect to health insurance coverage offered, sold, issued, renewed, in effect, or operated in the individual market after the date that is 1 year after the date of enactment of this Act.

SEC. 103. AMENDMENTS TO THE INTERNAL REVENUE CODE OF 1986.

(a) NO DISCRIMINATION IN GROUP PREMIUMS BASED ON GENETIC INFORMATION.—Subsection (b) of section 9802 of the Internal Revenue Code of 1986 is amended—

26 USC 9802.

(1) in paragraph (2)(A), by inserting before the semicolon the following: "except as provided in paragraph (3)"; and

(2) by adding at the end the following:

"(3) NO GROUP-BASED DISCRIMINATION ON BASIS OF GENETIC INFORMATION.—

"(A) IN GENERAL.—For purposes of this section, a group health plan may not adjust premium or contribution amounts for the group covered under such plan on the basis of genetic information.

"(B) RULE OF CONSTRUCTION.—Nothing in subparagraph (A) or in paragraphs (1) and (2) of subsection (d) shall be construed to limit the ability of a group health plan to increase the premium for an employer based on the manifestation of a disease or disorder of an individual who is enrolled in the plan. In such case, the manifestation of a disease or disorder in one individual cannot also be used as genetic information about other group members and to further increase the premium for the employer.".

(b) LIMITATIONS ON GENETIC TESTING; PROHIBITION ON COLLECTION OF GENETIC INFORMATION; APPLICATION TO ALL PLANS.—Section 9802 of such Code is amended by redesignating subsection (c) as subsection (f) and by inserting after subsection (b) the following new subsections:

"(c) GENETIC TESTING.—

"(1) LIMITATION ON REQUESTING OR REQUIRING GENETIC TESTING.—A group health plan may not request or require an individual or a family member of such individual to undergo a genetic test.

"(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to limit the authority of a health care professional who is providing health care services to an individual to request that such individual undergo a genetic test.

"(3) RULE OF CONSTRUCTION REGARDING PAYMENT.—

"(A) IN GENERAL.—Nothing in paragraph (1) shall be construed to preclude a group health plan from obtaining and using the results of a genetic test in making a determination regarding payment (as such term is defined for the purposes of applying the regulations promulgated by the Secretary of Health and Human Services under part C of title XI of the Social Security Act and section 264 of the Health Insurance Portability and Accountability Act of 1996, as may be revised from time to time) consistent with subsection (a).

"(B) LIMITATION.—For purposes of subparagraph (A), a group health plan may request only the minimum amount of information necessary to accomplish the intended purpose.

"(4) RESEARCH EXCEPTION.—Notwithstanding paragraph (1), a group health plan may request, but not require, that a participant or beneficiary undergo a genetic test if each of the following conditions is met:

"(A) The request is made pursuant to research that complies with part 46 of title 45, Code of Federal Regulations, or equivalent Federal regulations, and any applicable State or local law or regulations for the protection of human subjects in research.

"(B) The plan clearly indicates to each participant or beneficiary, or in the case of a minor child, to the legal guardian of such beneficiary, to whom the request is made that—

"(i) compliance with the request is voluntary; and

"(ii) non-compliance will have no effect on enrollment status or premium or contribution amounts.

"(C) No genetic information collected or acquired under this paragraph shall be used for underwriting purposes.

"(D) The plan notifies the Secretary in writing that the plan is conducting activities pursuant to the exception provided for under this paragraph, including a description of the activities conducted. Notification.

"(E) The plan complies with such other conditions as the Secretary may by regulation require for activities conducted under this paragraph.

"(d) PROHIBITION ON COLLECTION OF GENETIC INFORMATION.—

"(1) IN GENERAL.—A group health plan shall not request, require, or purchase genetic information for underwriting purposes (as defined in section 9832).

"(2) PROHIBITION ON COLLECTION OF GENETIC INFORMATION PRIOR TO ENROLLMENT.—A group health plan shall not request, require, or purchase genetic information with respect to any individual prior to such individual's enrollment under the plan or in connection with such enrollment.

"(3) INCIDENTAL COLLECTION.—If a group health plan obtains genetic information incidental to the requesting, requiring, or purchasing of other information concerning any individual, such request, requirement, or purchase shall not be considered a violation of paragraph (2) if such request, requirement, or purchase is not in violation of paragraph (1).

"(e) APPLICATION TO ALL PLANS.—The provisions of subsections (a)(1)(F), (b)(3), (c), and (d) and subsection (b)(1) and section 9801 with respect to genetic information, shall apply to group health plans without regard to section 9831(a)(2).".

(c) APPLICATION TO GENETIC INFORMATION OF A FETUS OR EMBRYO.—Such section is further amended by adding at the end the following:

"(f) GENETIC INFORMATION OF A FETUS OR EMBRYO.—Any reference in this chapter to genetic information concerning an individual or family member of an individual shall—

"(1) with respect to such an individual or family member of an individual who is a pregnant woman, include genetic

information of any fetus carried by such pregnant woman; and

"(2) with respect to an individual or family member utilizing an assisted reproductive technology, include genetic information of any embryo legally held by the individual or family member.".

26 USC 9832.

(d) DEFINITIONS.—Subsection (d) of section 9832 of such Code is amended by adding at the end the following:

"(6) FAMILY MEMBER.—The term 'family member' means, with respect to any individual—

"(A) a dependent (as such term is used for purposes of section 9801(f)(2)) of such individual, and

"(B) any other individual who is a first-degree, second-degree, third-degree, or fourth-degree relative of such individual or of an individual described in subparagraph (A).

"(7) GENETIC INFORMATION.—

"(A) IN GENERAL.—The term 'genetic information' means, with respect to any individual, information about—

"(i) such individual's genetic tests,

"(ii) the genetic tests of family members of such individual, and

"(iii) the manifestation of a disease or disorder in family members of such individual.

"(B) INCLUSION OF GENETIC SERVICES AND PARTICIPATION IN GENETIC RESEARCH.—Such term includes, with respect to any individual, any request for, or receipt of, genetic services, or participation in clinical research which includes genetic services, by such individual or any family member of such individual.

"(C) EXCLUSIONS.—The term 'genetic information' shall not include information about the sex or age of any individual.

"(8) GENETIC TEST.—

"(A) IN GENERAL.—The term 'genetic test' means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.

"(B) EXCEPTIONS.—The term 'genetic test' does not mean—

"(i) an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes, or

"(ii) an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

"(9) GENETIC SERVICES.—The term 'genetic services' means—

"(A) a genetic test;

"(B) genetic counseling (including obtaining, interpreting, or assessing genetic information); or

"(C) genetic education.

"(10) UNDERWRITING PURPOSES.—The term 'underwriting purposes' means, with respect to any group health plan, or health insurance coverage offered in connection with a group health plan—

"(A) rules for, or determination of, eligibility (including enrollment and continued eligibility) for benefits under the plan or coverage;

"(B) the computation of premium or contribution amounts under the plan or coverage;

"(C) the application of any pre-existing condition exclusion under the plan or coverage; and

"(D) other activities related to the creation, renewal, or replacement of a contract of health insurance or health benefits.".

(e) ENFORCEMENT.—

(1) IN GENERAL.—Subchapter C of chapter 100 of the Internal Revenue Code of 1986 (relating to general provisions) is amended by adding at the end the following new section:

"SEC. 9834. ENFORCEMENT.

"For the imposition of tax on any failure of a group health plan to meet the requirements of this chapter, see section 4980D.".

(2) CONFORMING AMENDMENT.—The table of sections for subchapter C of chapter 100 of such Code is amended by adding at the end the following new item:

"Sec. 9834. Enforcement.".

(f) REGULATIONS AND EFFECTIVE DATE.— 26 USC 9802 note.

(1) REGULATIONS.—The Secretary of the Treasury shall issue final regulations or other guidance not later than 12 months after the date of the enactment of this Act to carry out the amendments made by this section.

(2) EFFECTIVE DATE.—The amendments made by this section shall apply with respect to group health plans for plan years beginning after the date that is 1 year after the date of the enactment of this Act. Applicability.

SEC. 104. AMENDMENTS TO TITLE XVIII OF THE SOCIAL SECURITY ACT RELATING TO MEDIGAP.

(a) NONDISCRIMINATION.—Section 1882(s)(2) of the Social Security Act (42 U.S.C. 1395ss(s)(2)) is amended by adding at the end the following:

"(E) An issuer of a medicare supplemental policy shall not deny or condition the issuance or effectiveness of the policy (including the imposition of any exclusion of benefits under the policy based on a pre-existing condition) and shall not discriminate in the pricing of the policy (including the adjustment of premium rates) of an individual on the basis of the genetic information with respect to such individual.

"(F) RULE OF CONSTRUCTION.—Nothing in subparagraph (E) or in subparagraphs (A) or (B) of subsection (x)(2) shall be construed to limit the ability of an issuer of a medicare supplemental policy from, to the extent otherwise permitted under this title—

"(i) denying or conditioning the issuance or effectiveness of the policy or increasing the premium for an employer based on the manifestation of a disease or disorder of an individual who is covered under the policy; or

"(ii) increasing the premium for any policy issued to an individual based on the manifestation of a disease

or disorder of an individual who is covered under the policy (in such case, the manifestation of a disease or disorder in one individual cannot also be used as genetic information about other group members and to further increase the premium for the employer).".

(b) LIMITATIONS ON GENETIC TESTING AND GENETIC INFORMATION.—

(1) IN GENERAL.—Section 1882 of the Social Security Act (42 U.S.C. 1395ss) is amended by adding at the end the following:

"(x) LIMITATIONS ON GENETIC TESTING AND INFORMATION.—

"(1) GENETIC TESTING.—

"(A) LIMITATION ON REQUESTING OR REQUIRING GENETIC TESTING.—An issuer of a medicare supplemental policy shall not request or require an individual or a family member of such individual to undergo a genetic test.

"(B) RULE OF CONSTRUCTION.—Subparagraph (A) shall not be construed to limit the authority of a health care professional who is providing health care services to an individual to request that such individual undergo a genetic test.

"(C) RULE OF CONSTRUCTION REGARDING PAYMENT.—

"(i) IN GENERAL.—Nothing in subparagraph (A) shall be construed to preclude an issuer of a medicare supplemental policy from obtaining and using the results of a genetic test in making a determination regarding payment (as such term is defined for the purposes of applying the regulations promulgated by the Secretary under part C of title XI and section 264 of the Health Insurance Portability and Accountability Act of 1996, as may be revised from time to time) consistent with subsection (s)(2)(E).

"(ii) LIMITATION.—For purposes of clause (i), an issuer of a medicare supplemental policy may request only the minimum amount of information necessary to accomplish the intended purpose.

"(D) RESEARCH EXCEPTION.—Notwithstanding subparagraph (A), an issuer of a medicare supplemental policy may request, but not require, that an individual or a family member of such individual undergo a genetic test if each of the following conditions is met:

"(i) The request is made pursuant to research that complies with part 46 of title 45, Code of Federal Regulations, or equivalent Federal regulations, and any applicable State or local law or regulations for the protection of human subjects in research.

"(ii) The issuer clearly indicates to each individual, or in the case of a minor child, to the legal guardian of such child, to whom the request is made that—

"(I) compliance with the request is voluntary; and

"(II) non-compliance will have no effect on enrollment status or premium or contribution amounts.

"(iii) No genetic information collected or acquired under this subparagraph shall be used for underwriting, determination of eligibility to enroll or maintain enrollment status, premium rating, or the creation, renewal, or replacement of a plan, contract, or coverage for health insurance or health benefits.

"(iv) The issuer notifies the Secretary in writing that the issuer is conducting activities pursuant to the exception provided for under this subparagraph, including a description of the activities conducted.

"(v) The issuer complies with such other conditions as the Secretary may by regulation require for activities conducted under this subparagraph.

"(2) PROHIBITION ON COLLECTION OF GENETIC INFORMATION.—

"(A) IN GENERAL.—An issuer of a medicare supplemental policy shall not request, require, or purchase genetic information for underwriting purposes (as defined in paragraph (3)).

"(B) PROHIBITION ON COLLECTION OF GENETIC INFORMATION PRIOR TO ENROLLMENT.—An issuer of a medicare supplemental policy shall not request, require, or purchase genetic information with respect to any individual prior to such individual's enrollment under the policy in connection with such enrollment.

"(C) INCIDENTAL COLLECTION.—If an issuer of a medicare supplemental policy obtains genetic information incidental to the requesting, requiring, or purchasing of other information concerning any individual, such request, requirement, or purchase shall not be considered a violation of subparagraph (B) if such request, requirement, or purchase is not in violation of subparagraph (A).

"(3) DEFINITIONS.—In this subsection:

"(A) FAMILY MEMBER.—The term 'family member' means with respect to an individual, any other individual who is a first-degree, second-degree, third-degree, or fourth-degree relative of such individual.

"(B) GENETIC INFORMATION.—

"(i) IN GENERAL.—The term 'genetic information' means, with respect to any individual, information about—

"(I) such individual's genetic tests,

"(II) the genetic tests of family members of such individual, and

"(III) subject to clause (iv), the manifestation of a disease or disorder in family members of such individual.

"(ii) INCLUSION OF GENETIC SERVICES AND PARTICIPATION IN GENETIC RESEARCH.—Such term includes, with respect to any individual, any request for, or receipt of, genetic services, or participation in clinical research which includes genetic services, by such individual or any family member of such individual.

"(iii) EXCLUSIONS.—The term 'genetic information' shall not include information about the sex or age of any individual.

"(C) GENETIC TEST.—

"(i) IN GENERAL.—The term 'genetic test' means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.

"(ii) EXCEPTIONS.—The term 'genetic test' does not mean—

"(I) an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes; or

"(II) an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

"(D) GENETIC SERVICES.—The term 'genetic services' means—

"(i) a genetic test;

"(ii) genetic counseling (including obtaining, interpreting, or assessing genetic information); or

"(iii) genetic education.

"(E) UNDERWRITING PURPOSES.—The term 'underwriting purposes' means, with respect to a medicare supplemental policy—

"(i) rules for, or determination of, eligibility (including enrollment and continued eligibility) for benefits under the policy;

"(ii) the computation of premium or contribution amounts under the policy;

"(iii) the application of any pre-existing condition exclusion under the policy; and

"(iv) other activities related to the creation, renewal, or replacement of a contract of health insurance or health benefits.

"(F) ISSUER OF A MEDICARE SUPPLEMENTAL POLICY.—The term 'issuer of a medicare supplemental policy' includes a third-party administrator or other person acting for or on behalf of such issuer.".

(2) APPLICATION TO GENETIC INFORMATION OF A FETUS OR EMBRYO.—Section 1882(x) of such Act, as added by paragraph (1), is further amended by adding at the end the following:

"(4) GENETIC INFORMATION OF A FETUS OR EMBRYO.—Any reference in this section to genetic information concerning an individual or family member of an individual shall—

"(A) with respect to such an individual or family member of an individual who is a pregnant woman, include genetic information of any fetus carried by such pregnant woman; and

"(B) with respect to an individual or family member utilizing an assisted reproductive technology, include genetic information of any embryo legally held by the individual or family member.".

(3) CONFORMING AMENDMENT.—Section 1882(o) of the Social Security Act (42 U.S.C. 1395ss(o)) is amended by adding at the end the following:

"(4) The issuer of the medicare supplemental policy complies with subsection (s)(2)(E) and subsection (x).".

(c) EFFECTIVE DATE.—The amendments made by this section shall apply with respect to an issuer of a medicare supplemental policy for policy years beginning on or after the date that is 1 year after the date of enactment of this Act. Applicability. 42 USC 1395ss note.

(d) TRANSITION PROVISIONS.— 42 USC 1395ss note.

(1) IN GENERAL.—If the Secretary of Health and Human Services identifies a State as requiring a change to its statutes or regulations to conform its regulatory program to the changes made by this section, the State regulatory program shall not be considered to be out of compliance with the requirements of section 1882 of the Social Security Act due solely to failure to make such change until the date specified in paragraph (4).

(2) NAIC STANDARDS.—If, not later than October 31, 2008, the National Association of Insurance Commissioners (in this subsection referred to as the "NAIC") modifies its NAIC Model Regulation relating to section 1882 of the Social Security Act (referred to in such section as the 1991 NAIC Model Regulation, as subsequently modified) to conform to the amendments made by this section, such revised regulation incorporating the modifications shall be considered to be the applicable NAIC model regulation (including the revised NAIC model regulation and the 1991 NAIC Model Regulation) for the purposes of such section. Deadline.

(3) SECRETARY STANDARDS.—If the NAIC does not make the modifications described in paragraph (2) within the period specified in such paragraph, the Secretary of Health and Human Services shall, not later than July 1, 2009, make the modifications described in such paragraph and such revised regulation incorporating the modifications shall be considered to be the appropriate regulation for the purposes of such section. Deadline.

(4) DATE SPECIFIED.—

(A) IN GENERAL.—Subject to subparagraph (B), the date specified in this paragraph for a State is the earlier of—

(i) the date the State changes its statutes or regulations to conform its regulatory program to the changes made by this section, or

(ii) July 1, 2009.

(B) ADDITIONAL LEGISLATIVE ACTION REQUIRED.—In the case of a State which the Secretary identifies as—

(i) requiring State legislation (other than legislation appropriating funds) to conform its regulatory program to the changes made in this section, but

(ii) having a legislature which is not scheduled to meet in 2009 in a legislative session in which such legislation may be considered, the date specified in this paragraph is the first day of the first calendar quarter beginning after the close of the first legislative session of the State legislature that begins on or after July 1, 2009. For purposes of the previous sentence, in the case of a State that has a 2-year legislative session, each year of such session shall be deemed to be a separate regular session of the State legislature.

SEC. 105. PRIVACY AND CONFIDENTIALITY.

(a) IN GENERAL.—Part C of title XI of the Social Security Act is amended by adding at the end the following new section:

"APPLICATION OF HIPAA REGULATIONS TO GENETIC INFORMATION

42 USC 1320d–9.

"SEC. 1180. (a) IN GENERAL.—The Secretary shall revise the HIPAA privacy regulation (as defined in subsection (b)) so it is consistent with the following:

"(1) Genetic information shall be treated as health information described in section 1171(4)(B).

"(2) The use or disclosure by a covered entity that is a group health plan, health insurance issuer that issues health insurance coverage, or issuer of a medicare supplemental policy of protected health information that is genetic information about an individual for underwriting purposes under the group health plan, health insurance coverage, or medicare supplemental policy shall not be a permitted use or disclosure.

"(b) DEFINITIONS.—For purposes of this section:

"(1) GENETIC INFORMATION; GENETIC TEST; FAMILY MEMBER.—The terms 'genetic information', 'genetic test', and 'family member' have the meanings given such terms in section 2791 of the Public Health Service Act (42 U.S.C. 300gg–91), as amended by the Genetic Information Nondiscrimination Act of 2007.

"(2) GROUP HEALTH PLAN; HEALTH INSURANCE COVERAGE; MEDICARE SUPPLEMENTAL POLICY.—The terms 'group health plan' and 'health insurance coverage' have the meanings given such terms under section 2791 of the Public Health Service Act (42 U.S.C. 300gg–91), and the term 'medicare supplemental policy' has the meaning given such term in section 1882(g).

"(3) HIPAA PRIVACY REGULATION.—The term 'HIPAA privacy regulation' means the regulations promulgated by the Secretary under this part and section 264 of the Health Insurance Portability and Accountability Act of 1996 (42 U.S.C. 1320d–2 note).

"(4) UNDERWRITING PURPOSES.—The term 'underwriting purposes' means, with respect to a group health plan, health insurance coverage, or a medicare supplemental policy—

"(A) rules for, or determination of, eligibility (including enrollment and continued eligibility) for, or determination of, benefits under the plan, coverage, or policy;

"(B) the computation of premium or contribution amounts under the plan, coverage, or policy;

"(C) the application of any pre-existing condition exclusion under the plan, coverage, or policy; and

"(D) other activities related to the creation, renewal, or replacement of a contract of health insurance or health benefits.

Notice.
Federal Register, publication.
Deadline.
Effective date.

"(c) PROCEDURE.—The revisions under subsection (a) shall be made by notice in the Federal Register published not later than 60 days after the date of the enactment of this section and shall be effective upon publication, without opportunity for any prior public comment, but may be revised, consistent with this section, after opportunity for public comment.

"(d) ENFORCEMENT.—In addition to any other sanctions or remedies that may be available under law, a covered entity that is a group health plan, health insurance issuer, or issuer of a medicare supplemental policy and that violates the HIPAA privacy regulation (as revised under subsection (a) or otherwise) with respect to the use or disclosure of genetic information shall be subject to the

penalties described in sections 1176 and 1177 in the same manner and to the same extent that such penalties apply to violations of this part.”.

(b) REGULATIONS; EFFECTIVE DATE.— 42 USC 1320d–9 note. Deadline.

(1) REGULATIONS.—Not later than 12 months after the date of the enactment of this Act, the Secretary of Health and Human Services shall issue final regulations to carry out the revision required by section 1180(a) of the Social Security Act, as added by subsection (a). The Secretary has the sole authority to promulgate such regulations, but shall promulgate such regulations in consultation with the Secretaries of Labor and the Treasury.

(2) EFFECTIVE DATE.—The amendment made by subsection (a) shall take effect on the date that is 1 year after the date of the enactment of this Act.

SEC. 106. ASSURING COORDINATION.

Memorandum. 42 USC 300gg–1 note.

Except as provided in section 105(b)(1), the Secretary of Health and Human Services, the Secretary of Labor, and the Secretary of the Treasury shall ensure, through the execution of an interagency memorandum of understanding among such Secretaries, that—

(1) regulations, rulings, and interpretations issued by such Secretaries relating to the same matter over which two or more such Secretaries have responsibility under this title (and the amendments made by this title) are administered so as to have the same effect at all times; and

(2) coordination of policies relating to enforcing the same requirements through such Secretaries in order to have a coordinated enforcement strategy that avoids duplication of enforcement efforts and assigns priorities in enforcement.

TITLE II—PROHIBITING EMPLOYMENT DISCRIMINATION ON THE BASIS OF GENETIC INFORMATION

SEC. 201. DEFINITIONS.

42 USC 2000ff.

In this title:

(1) COMMISSION.—The term “Commission” means the Equal Employment Opportunity Commission as created by section 705 of the Civil Rights Act of 1964 (42 U.S.C. 2000e–4).

(2) EMPLOYEE; EMPLOYER; EMPLOYMENT AGENCY; LABOR ORGANIZATION; MEMBER.—

(A) IN GENERAL.—The term “employee” means—

(i) an employee (including an applicant), as defined in section 701(f) of the Civil Rights Act of 1964 (42 U.S.C. 2000e(f));

(ii) a State employee (including an applicant) described in section 304(a) of the Government Employee Rights Act of 1991 (42 U.S.C. 2000e–16c(a));

(iii) a covered employee (including an applicant), as defined in section 101 of the Congressional Accountability Act of 1995 (2 U.S.C. 1301);

(iv) a covered employee (including an applicant), as defined in section 411(c) of title 3, United States Code; or

(v) an employee or applicant to which section 717(a) of the Civil Rights Act of 1964 (42 U.S.C. 2000e–16(a)) applies.

(B) EMPLOYER.—The term "employer" means—

(i) an employer (as defined in section 701(b) of the Civil Rights Act of 1964 (42 U.S.C. 2000e(b)));

(ii) an entity employing a State employee described in section 304(a) of the Government Employee Rights Act of 1991;

(iii) an employing office, as defined in section 101 of the Congressional Accountability Act of 1995;

(iv) an employing office, as defined in section 411(c) of title 3, United States Code; or

(v) an entity to which section 717(a) of the Civil Rights Act of 1964 applies.

(C) EMPLOYMENT AGENCY; LABOR ORGANIZATION.—The terms "employment agency" and "labor organization" have the meanings given the terms in section 701 of the Civil Rights Act of 1964 (42 U.S.C. 2000e).

(D) MEMBER.—The term "member", with respect to a labor organization, includes an applicant for membership in a labor organization.

(3) FAMILY MEMBER.—The term "family member" means, with respect to an individual—

(A) a dependent (as such term is used for purposes of section 701(f)(2) of the Employee Retirement Income Security Act of 1974) of such individual, and

(B) any other individual who is a first-degree, second-degree, third-degree, or fourth-degree relative of such individual or of an individual described in subparagraph (A).

(4) GENETIC INFORMATION.—

(A) IN GENERAL.—The term "genetic information" means, with respect to any individual, information about—

(i) such individual's genetic tests,

(ii) the genetic tests of family members of such individual, and

(iii) the manifestation of a disease or disorder in family members of such individual.

(B) INCLUSION OF GENETIC SERVICES AND PARTICIPATION IN GENETIC RESEARCH.—Such term includes, with respect to any individual, any request for, or receipt of, genetic services, or participation in clinical research which includes genetic services, by such individual or any family member of such individual.

(C) EXCLUSIONS.—The term "genetic information" shall not include information about the sex or age of any individual.

(5) GENETIC MONITORING.—The term "genetic monitoring" means the periodic examination of employees to evaluate acquired modifications to their genetic material, such as chromosomal damage or evidence of increased occurrence of mutations, that may have developed in the course of employment due to exposure to toxic substances in the workplace,

in order to identify, evaluate, and respond to the effects of or control adverse environmental exposures in the workplace.

(6) GENETIC SERVICES.—The term "genetic services" means—

(A) a genetic test;

(B) genetic counseling (including obtaining, interpreting, or assessing genetic information); or

(C) genetic education.

(7) GENETIC TEST.—

(A) IN GENERAL.—The term "genetic test" means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.

(B) EXCEPTIONS.—The term "genetic test" does not mean an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes.

SEC. 202. EMPLOYER PRACTICES. 42 USC 2000ff–1.

(a) DISCRIMINATION BASED ON GENETIC INFORMATION.—It shall be an unlawful employment practice for an employer—

(1) to fail or refuse to hire, or to discharge, any employee, or otherwise to discriminate against any employee with respect to the compensation, terms, conditions, or privileges of employment of the employee, because of genetic information with respect to the employee; or

(2) to limit, segregate, or classify the employees of the employer in any way that would deprive or tend to deprive any employee of employment opportunities or otherwise adversely affect the status of the employee as an employee, because of genetic information with respect to the employee.

(b) ACQUISITION OF GENETIC INFORMATION.—It shall be an unlawful employment practice for an employer to request, require, or purchase genetic information with respect to an employee or a family member of the employee except—

(1) where an employer inadvertently requests or requires family medical history of the employee or family member of the employee;

(2) where—

(A) health or genetic services are offered by the employer, including such services offered as part of a wellness program;

(B) the employee provides prior, knowing, voluntary, and written authorization;

(C) only the employee (or family member if the family member is receiving genetic services) and the licensed health care professional or board certified genetic counselor involved in providing such services receive individually identifiable information concerning the results of such services; and

(D) any individually identifiable genetic information provided under subparagraph (C) in connection with the services provided under subparagraph (A) is only available for purposes of such services and shall not be disclosed to the employer except in aggregate terms that do not disclose the identity of specific employees;

(3) where an employer requests or requires family medical history from the employee to comply with the certification

provisions of section 103 of the Family and Medical Leave Act of 1993 (29 U.S.C. 2613) or such requirements under State family and medical leave laws;

(4) where an employer purchases documents that are commercially and publicly available (including newspapers, magazines, periodicals, and books, but not including medical databases or court records) that include family medical history;

(5) where the information involved is to be used for genetic monitoring of the biological effects of toxic substances in the workplace, but only if—

(A) the employer provides written notice of the genetic monitoring to the employee;

(B)(i) the employee provides prior, knowing, voluntary, and written authorization; or

(ii) the genetic monitoring is required by Federal or State law;

(C) the employee is informed of individual monitoring results;

(D) the monitoring is in compliance with—

(i) any Federal genetic monitoring regulations, including any such regulations that may be promulgated by the Secretary of Labor pursuant to the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.), the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 801 et seq.), or the Atomic Energy Act of 1954 (42 U.S.C. 2011 et seq.); or

(ii) State genetic monitoring regulations, in the case of a State that is implementing genetic monitoring regulations under the authority of the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.); and

(E) the employer, excluding any licensed health care professional or board certified genetic counselor that is involved in the genetic monitoring program, receives the results of the monitoring only in aggregate terms that do not disclose the identity of specific employees; or

(6) where the employer conducts DNA analysis for law enforcement purposes as a forensic laboratory or for purposes of human remains identification, and requests or requires genetic information of such employer's employees, but only to the extent that such genetic information is used for analysis of DNA identification markers for quality control to detect sample contamination.

(c) PRESERVATION OF PROTECTIONS.—In the case of information to which any of paragraphs (1) through (6) of subsection (b) applies, such information may not be used in violation of paragraph (1) or (2) of subsection (a) or treated or disclosed in a manner that violates section 206.

42 USC 2000ff–2.

SEC. 203. EMPLOYMENT AGENCY PRACTICES.

(a) DISCRIMINATION BASED ON GENETIC INFORMATION.—It shall be an unlawful employment practice for an employment agency—

(1) to fail or refuse to refer for employment, or otherwise to discriminate against, any individual because of genetic information with respect to the individual;

(2) to limit, segregate, or classify individuals or fail or refuse to refer for employment any individual in any way

that would deprive or tend to deprive any individual of employment opportunities, or otherwise adversely affect the status of the individual as an employee, because of genetic information with respect to the individual; or

(3) to cause or attempt to cause an employer to discriminate against an individual in violation of this title.

(b) ACQUISITION OF GENETIC INFORMATION.—It shall be an unlawful employment practice for an employment agency to request, require, or purchase genetic information with respect to an individual or a family member of the individual except—

(1) where an employment agency inadvertently requests or requires family medical history of the individual or family member of the individual;

(2) where—

(A) health or genetic services are offered by the employment agency, including such services offered as part of a wellness program;

(B) the individual provides prior, knowing, voluntary, and written authorization;

(C) only the individual (or family member if the family member is receiving genetic services) and the licensed health care professional or board certified genetic counselor involved in providing such services receive individually identifiable information concerning the results of such services; and

(D) any individually identifiable genetic information provided under subparagraph (C) in connection with the services provided under subparagraph (A) is only available for purposes of such services and shall not be disclosed to the employment agency except in aggregate terms that do not disclose the identity of specific individuals;

(3) where an employment agency requests or requires family medical history from the individual to comply with the certification provisions of section 103 of the Family and Medical Leave Act of 1993 (29 U.S.C. 2613) or such requirements under State family and medical leave laws;

(4) where an employment agency purchases documents that are commercially and publicly available (including newspapers, magazines, periodicals, and books, but not including medical databases or court records) that include family medical history; or

(5) where the information involved is to be used for genetic monitoring of the biological effects of toxic substances in the workplace, but only if—

(A) the employment agency provides written notice of the genetic monitoring to the individual;

(B)(i) the individual provides prior, knowing, voluntary, and written authorization; or

(ii) the genetic monitoring is required by Federal or State law;

(C) the individual is informed of individual monitoring results;

(D) the monitoring is in compliance with—

(i) any Federal genetic monitoring regulations, including any such regulations that may be promulgated by the Secretary of Labor pursuant to the Occupational Safety and Health Act of 1970 (29 U.S.C.

651 et seq.), the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 801 et seq.), or the Atomic Energy Act of 1954 (42 U.S.C. 2011 et seq.); or

(ii) State genetic monitoring regulations, in the case of a State that is implementing genetic monitoring regulations under the authority of the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.); and

(E) the employment agency, excluding any licensed health care professional or board certified genetic counselor that is involved in the genetic monitoring program, receives the results of the monitoring only in aggregate terms that do not disclose the identity of specific individuals.

(c) PRESERVATION OF PROTECTIONS.—In the case of information to which any of paragraphs (1) through (5) of subsection (b) applies, such information may not be used in violation of paragraph (1), (2), or (3) of subsection (a) or treated or disclosed in a manner that violates section 206.

42 USC 2000ff–3.

SEC. 204. LABOR ORGANIZATION PRACTICES.

(a) DISCRIMINATION BASED ON GENETIC INFORMATION.—It shall be an unlawful employment practice for a labor organization—

(1) to exclude or to expel from the membership of the organization, or otherwise to discriminate against, any member because of genetic information with respect to the member;

(2) to limit, segregate, or classify the members of the organization, or fail or refuse to refer for employment any member, in any way that would deprive or tend to deprive any member of employment opportunities, or otherwise adversely affect the status of the member as an employee, because of genetic information with respect to the member; or

(3) to cause or attempt to cause an employer to discriminate against a member in violation of this title.

(b) ACQUISITION OF GENETIC INFORMATION.—It shall be an unlawful employment practice for a labor organization to request, require, or purchase genetic information with respect to a member or a family member of the member except—

(1) where a labor organization inadvertently requests or requires family medical history of the member or family member of the member;

(2) where—

(A) health or genetic services are offered by the labor organization, including such services offered as part of a wellness program;

(B) the member provides prior, knowing, voluntary, and written authorization;

(C) only the member (or family member if the family member is receiving genetic services) and the licensed health care professional or board certified genetic counselor involved in providing such services receive individually identifiable information concerning the results of such services; and

(D) any individually identifiable genetic information provided under subparagraph (C) in connection with the services provided under subparagraph (A) is only available for purposes of such services and shall not be disclosed

to the labor organization except in aggregate terms that do not disclose the identity of specific members;

(3) where a labor organization requests or requires family medical history from the members to comply with the certification provisions of section 103 of the Family and Medical Leave Act of 1993 (29 U.S.C. 2613) or such requirements under State family and medical leave laws;

(4) where a labor organization purchases documents that are commercially and publicly available (including newspapers, magazines, periodicals, and books, but not including medical databases or court records) that include family medical history; or

(5) where the information involved is to be used for genetic monitoring of the biological effects of toxic substances in the workplace, but only if—

(A) the labor organization provides written notice of the genetic monitoring to the member;

(B)(i) the member provides prior, knowing, voluntary, and written authorization; or

(ii) the genetic monitoring is required by Federal or State law;

(C) the member is informed of individual monitoring results;

(D) the monitoring is in compliance with—

(i) any Federal genetic monitoring regulations, including any such regulations that may be promulgated by the Secretary of Labor pursuant to the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.), the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 801 et seq.), or the Atomic Energy Act of 1954 (42 U.S.C. 2011 et seq.); or

(ii) State genetic monitoring regulations, in the case of a State that is implementing genetic monitoring regulations under the authority of the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.); and

(E) the labor organization, excluding any licensed health care professional or board certified genetic counselor that is involved in the genetic monitoring program, receives the results of the monitoring only in aggregate terms that do not disclose the identity of specific members.

(c) PRESERVATION OF PROTECTIONS.—In the case of information to which any of paragraphs (1) through (5) of subsection (b) applies, such information may not be used in violation of paragraph (1), (2), or (3) of subsection (a) or treated or disclosed in a manner that violates section 206.

SEC. 205. TRAINING PROGRAMS. 42 USC 2000ff–4.

(a) DISCRIMINATION BASED ON GENETIC INFORMATION.—It shall be an unlawful employment practice for any employer, labor organization, or joint labor-management committee controlling apprenticeship or other training or retraining, including on-the-job training programs—

(1) to discriminate against any individual because of genetic information with respect to the individual in admission to, or employment in, any program established to provide apprenticeship or other training or retraining;

(2) to limit, segregate, or classify the applicants for or participants in such apprenticeship or other training or retraining, or fail or refuse to refer for employment any individual, in any way that would deprive or tend to deprive any individual of employment opportunities, or otherwise adversely affect the status of the individual as an employee, because of genetic information with respect to the individual; or

(3) to cause or attempt to cause an employer to discriminate against an applicant for or a participant in such apprenticeship or other training or retraining in violation of this title.

(b) ACQUISITION OF GENETIC INFORMATION.—It shall be an unlawful employment practice for an employer, labor organization, or joint labor-management committee described in subsection (a) to request, require, or purchase genetic information with respect to an individual or a family member of the individual except—

(1) where the employer, labor organization, or joint labor-management committee inadvertently requests or requires family medical history of the individual or family member of the individual;

(2) where—

(A) health or genetic services are offered by the employer, labor organization, or joint labor-management committee, including such services offered as part of a wellness program;

(B) the individual provides prior, knowing, voluntary, and written authorization;

(C) only the individual (or family member if the family member is receiving genetic services) and the licensed health care professional or board certified genetic counselor involved in providing such services receive individually identifiable information concerning the results of such services; and

(D) any individually identifiable genetic information provided under subparagraph (C) in connection with the services provided under subparagraph (A) is only available for purposes of such services and shall not be disclosed to the employer, labor organization, or joint labor-management committee except in aggregate terms that do not disclose the identity of specific individuals;

(3) where the employer, labor organization, or joint labor-management committee requests or requires family medical history from the individual to comply with the certification provisions of section 103 of the Family and Medical Leave Act of 1993 (29 U.S.C. 2613) or such requirements under State family and medical leave laws;

(4) where the employer, labor organization, or joint labor-management committee purchases documents that are commercially and publicly available (including newspapers, magazines, periodicals, and books, but not including medical databases or court records) that include family medical history;

(5) where the information involved is to be used for genetic monitoring of the biological effects of toxic substances in the workplace, but only if—

Notification.

(A) the employer, labor organization, or joint labor-management committee provides written notice of the genetic monitoring to the individual;

(B)(i) the individual provides prior, knowing, voluntary, and written authorization; or

(ii) the genetic monitoring is required by Federal or State law;

(C) the individual is informed of individual monitoring results;

(D) the monitoring is in compliance with—

(i) any Federal genetic monitoring regulations, including any such regulations that may be promulgated by the Secretary of Labor pursuant to the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.), the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 801 et seq.), or the Atomic Energy Act of 1954 (42 U.S.C. 2011 et seq.); or

(ii) State genetic monitoring regulations, in the case of a State that is implementing genetic monitoring regulations under the authority of the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.); and

(E) the employer, labor organization, or joint labor-management committee, excluding any licensed health care professional or board certified genetic counselor that is involved in the genetic monitoring program, receives the results of the monitoring only in aggregate terms that do not disclose the identity of specific individuals; or

(6) where the employer conducts DNA analysis for law enforcement purposes as a forensic laboratory or for purposes of human remains identification, and requests or requires genetic information of such employer's apprentices or trainees, but only to the extent that such genetic information is used for analysis of DNA identification markers for quality control to detect sample contamination.

(c) PRESERVATION OF PROTECTIONS.—In the case of information to which any of paragraphs (1) through (6) of subsection (b) applies, such information may not be used in violation of paragraph (1), (2), or (3) of subsection (a) or treated or disclosed in a manner that violates section 206.

SEC. 206. CONFIDENTIALITY OF GENETIC INFORMATION. 42 USC 2000ff–5.

(a) TREATMENT OF INFORMATION AS PART OF CONFIDENTIAL MEDICAL RECORD.—If an employer, employment agency, labor organization, or joint labor-management committee possesses genetic information about an employee or member, such information shall be maintained on separate forms and in separate medical files and be treated as a confidential medical record of the employee or member. An employer, employment agency, labor organization, or joint labor-management committee shall be considered to be in compliance with the maintenance of information requirements of this subsection with respect to genetic information subject to this subsection that is maintained with and treated as a confidential medical record under section 102(d)(3)(B) of the Americans With Disabilities Act (42 U.S.C. 12112(d)(3)(B)).

(b) LIMITATION ON DISCLOSURE.—An employer, employment agency, labor organization, or joint labor-management committee shall not disclose genetic information concerning an employee or member except—

(1) to the employee or member of a labor organization (or family member if the family member is receiving the genetic services) at the written request of the employee or member of such organization;

(2) to an occupational or other health researcher if the research is conducted in compliance with the regulations and protections provided for under part 46 of title 45, Code of Federal Regulations;

(3) in response to an order of a court, except that—

(A) the employer, employment agency, labor organization, or joint labor-management committee may disclose only the genetic information expressly authorized by such order; and

(B) if the court order was secured without the knowledge of the employee or member to whom the information refers, the employer, employment agency, labor organization, or joint labor-management committee shall inform the employee or member of the court order and any genetic information that was disclosed pursuant to such order;

(4) to government officials who are investigating compliance with this title if the information is relevant to the investigation;

(5) to the extent that such disclosure is made in connection with the employee's compliance with the certification provisions of section 103 of the Family and Medical Leave Act of 1993 (29 U.S.C. 2613) or such requirements under State family and medical leave laws; or

(6) to a Federal, State, or local public health agency only with regard to information that is described in section 201(4)(A)(iii) and that concerns a contagious disease that presents an imminent hazard of death or life-threatening illness, and that the employee whose family member or family members is or are the subject of a disclosure under this paragraph is notified of such disclosure.

(c) RELATIONSHIP TO HIPAA REGULATIONS.—With respect to the regulations promulgated by the Secretary of Health and Human Services under part C of title XI of the Social Security Act (42 U.S.C. 1320d et seq.) and section 264 of the Health Insurance Portability and Accountability Act of 1996 (42 U.S.C. 1320d–2 note), this title does not prohibit a covered entity under such regulations from any use or disclosure of health information that is authorized for the covered entity under such regulations. The previous sentence does not affect the authority of such Secretary to modify such regulations.

42 USC 2000ff–6.

SEC. 207. REMEDIES AND ENFORCEMENT.

(a) EMPLOYEES COVERED BY TITLE VII OF THE CIVIL RIGHTS ACT OF 1964.—

(1) IN GENERAL.—The powers, procedures, and remedies provided in sections 705, 706, 707, 709, 710, and 711 of the Civil Rights Act of 1964 (42 U.S.C. 2000e–4 et seq.) to the Commission, the Attorney General, or any person, alleging a violation of title VII of that Act (42 U.S.C. 2000e et seq.) shall be the powers, procedures, and remedies this title provides to the Commission, the Attorney General, or any person, respectively, alleging an unlawful employment practice in violation of this title against an employee described in section 201(2)(A)(i), except as provided in paragraphs (2) and (3).

(2) COSTS AND FEES.—The powers, remedies, and procedures provided in subsections (b) and (c) of section 722 of the Revised Statutes of the United States (42 U.S.C. 1988), shall be powers, remedies, and procedures this title provides to the Commission, the Attorney General, or any person, alleging such a practice.

(3) DAMAGES.—The powers, remedies, and procedures provided in section 1977A of the Revised Statutes of the United States (42 U.S.C. 1981a), including the limitations contained in subsection (b)(3) of such section 1977A, shall be powers, remedies, and procedures this title provides to the Commission, the Attorney General, or any person, alleging such a practice (not an employment practice specifically excluded from coverage under section 1977A(a)(1) of the Revised Statutes of the United States).

(b) EMPLOYEES COVERED BY GOVERNMENT EMPLOYEE RIGHTS ACT OF 1991.—

(1) IN GENERAL.—The powers, remedies, and procedures provided in sections 302 and 304 of the Government Employee Rights Act of 1991 (42 U.S.C. 2000e–16b, 2000e–16c) to the Commission, or any person, alleging a violation of section 302(a)(1) of that Act (42 U.S.C. 2000e–16b(a)(1)) shall be the powers, remedies, and procedures this title provides to the Commission, or any person, respectively, alleging an unlawful employment practice in violation of this title against an employee described in section 201(2)(A)(ii), except as provided in paragraphs (2) and (3).

(2) COSTS AND FEES.—The powers, remedies, and procedures provided in subsections (b) and (c) of section 722 of the Revised Statutes of the United States (42 U.S.C. 1988), shall be powers, remedies, and procedures this title provides to the Commission, or any person, alleging such a practice.

(3) DAMAGES.—The powers, remedies, and procedures provided in section 1977A of the Revised Statutes of the United States (42 U.S.C. 1981a), including the limitations contained in subsection (b)(3) of such section 1977A, shall be powers, remedies, and procedures this title provides to the Commission, or any person, alleging such a practice (not an employment practice specifically excluded from coverage under section 1977A(a)(1) of the Revised Statutes of the United States).

(c) EMPLOYEES COVERED BY CONGRESSIONAL ACCOUNTABILITY ACT OF 1995.—

(1) IN GENERAL.—The powers, remedies, and procedures provided in the Congressional Accountability Act of 1995 (2 U.S.C. 1301 et seq.) to the Board (as defined in section 101 of that Act (2 U.S.C. 1301)), or any person, alleging a violation of section 201(a)(1) of that Act (42 U.S.C. 1311(a)(1)) shall be the powers, remedies, and procedures this title provides to that Board, or any person, alleging an unlawful employment practice in violation of this title against an employee described in section 201(2)(A)(iii), except as provided in paragraphs (2) and (3).

(2) COSTS AND FEES.—The powers, remedies, and procedures provided in subsections (b) and (c) of section 722 of the Revised Statutes of the United States (42 U.S.C. 1988), shall be powers, remedies, and procedures this title provides to that Board, or any person, alleging such a practice.

(3) DAMAGES.—The powers, remedies, and procedures provided in section 1977A of the Revised Statutes of the United States (42 U.S.C. 1981a), including the limitations contained in subsection (b)(3) of such section 1977A, shall be powers, remedies, and procedures this title provides to that Board, or any person, alleging such a practice (not an employment practice specifically excluded from coverage under section 1977A(a)(1) of the Revised Statutes of the United States).

(4) OTHER APPLICABLE PROVISIONS.—With respect to a claim alleging a practice described in paragraph (1), title III of the Congressional Accountability Act of 1995 (2 U.S.C. 1381 et seq.) shall apply in the same manner as such title applies with respect to a claim alleging a violation of section 201(a)(1) of such Act (2 U.S.C. 1311(a)(1)).

(d) EMPLOYEES COVERED BY CHAPTER 5 OF TITLE 3, UNITED STATES CODE.—

(1) IN GENERAL.—The powers, remedies, and procedures provided in chapter 5 of title 3, United States Code, to the President, the Commission, the Merit Systems Protection Board, or any person, alleging a violation of section 411(a)(1) of that title, shall be the powers, remedies, and procedures this title provides to the President, the Commission, such Board, or any person, respectively, alleging an unlawful employment practice in violation of this title against an employee described in section 201(2)(A)(iv), except as provided in paragraphs (2) and (3).

(2) COSTS AND FEES.—The powers, remedies, and procedures provided in subsections (b) and (c) of section 722 of the Revised Statutes of the United States (42 U.S.C. 1988), shall be powers, remedies, and procedures this title provides to the President, the Commission, such Board, or any person, alleging such a practice.

(3) DAMAGES.—The powers, remedies, and procedures provided in section 1977A of the Revised Statutes of the United States (42 U.S.C. 1981a), including the limitations contained in subsection (b)(3) of such section 1977A, shall be powers, remedies, and procedures this title provides to the President, the Commission, such Board, or any person, alleging such a practice (not an employment practice specifically excluded from coverage under section 1977A(a)(1) of the Revised Statutes of the United States).

(e) EMPLOYEES COVERED BY SECTION 717 OF THE CIVIL RIGHTS ACT OF 1964.—

(1) IN GENERAL.—The powers, remedies, and procedures provided in section 717 of the Civil Rights Act of 1964 (42 U.S.C. 2000e–16) to the Commission, the Attorney General, the Librarian of Congress, or any person, alleging a violation of that section shall be the powers, remedies, and procedures this title provides to the Commission, the Attorney General, the Librarian of Congress, or any person, respectively, alleging an unlawful employment practice in violation of this title against an employee or applicant described in section 201(2)(A)(v), except as provided in paragraphs (2) and (3).

(2) COSTS AND FEES.—The powers, remedies, and procedures provided in subsections (b) and (c) of section 722 of the Revised Statutes of the United States (42 U.S.C. 1988), shall be powers, remedies, and procedures this title provides

to the Commission, the Attorney General, the Librarian of Congress, or any person, alleging such a practice.

(3) DAMAGES.—The powers, remedies, and procedures provided in section 1977A of the Revised Statutes of the United States (42 U.S.C. 1981a), including the limitations contained in subsection (b)(3) of such section 1977A, shall be powers, remedies, and procedures this title provides to the Commission, the Attorney General, the Librarian of Congress, or any person, alleging such a practice (not an employment practice specifically excluded from coverage under section 1977A(a)(1) of the Revised Statutes of the United States).

(f) PROHIBITION AGAINST RETALIATION.—No person shall discriminate against any individual because such individual has opposed any act or practice made unlawful by this title or because such individual made a charge, testified, assisted, or participated in any manner in an investigation, proceeding, or hearing under this title. The remedies and procedures otherwise provided for under this section shall be available to aggrieved individuals with respect to violations of this subsection.

(g) DEFINITION.—In this section, the term "Commission" means the Equal Employment Opportunity Commission.

SEC. 208. DISPARATE IMPACT. 42 USC 2000ff–7.

(a) GENERAL RULE.—Notwithstanding any other provision of this Act, "disparate impact", as that term is used in section 703(k) of the Civil Rights Act of 1964 (42 U.S.C. 2000e–2(k)), on the basis of genetic information does not establish a cause of action under this Act.

(b) COMMISSION.—On the date that is 6 years after the date of enactment of this Act, there shall be established a commission, to be known as the Genetic Nondiscrimination Study Commission (referred to in this section as the "Commission") to review the developing science of genetics and to make recommendations to Congress regarding whether to provide a disparate impact cause of action under this Act. Effective date. Establishment.

(c) MEMBERSHIP.—

(1) IN GENERAL.—The Commission shall be composed of 8 members, of which—

(A) 1 member shall be appointed by the Majority Leader of the Senate;

(B) 1 member shall be appointed by the Minority Leader of the Senate;

(C) 1 member shall be appointed by the Chairman of the Committee on Health, Education, Labor, and Pensions of the Senate;

(D) 1 member shall be appointed by the ranking minority member of the Committee on Health, Education, Labor, and Pensions of the Senate;

(E) 1 member shall be appointed by the Speaker of the House of Representatives;

(F) 1 member shall be appointed by the Minority Leader of the House of Representatives;

(G) 1 member shall be appointed by the Chairman of the Committee on Education and Labor of the House of Representatives; and

(H) 1 member shall be appointed by the ranking minority member of the Committee on Education and Labor of the House of Representatives.

(2) COMPENSATION AND EXPENSES.—The members of the Commission shall not receive compensation for the performance of services for the Commission, but shall be allowed travel expenses, including per diem in lieu of subsistence, at rates authorized for employees of agencies under subchapter I of chapter 57 of title 5, United States Code, while away from their homes or regular places of business in the performance of services for the Commission.

(d) ADMINISTRATIVE PROVISIONS.—

(1) LOCATION.—The Commission shall be located in a facility maintained by the Equal Employment Opportunity Commission.

(2) DETAIL OF GOVERNMENT EMPLOYEES.—Any Federal Government employee may be detailed to the Commission without reimbursement, and such detail shall be without interruption or loss of civil service status or privilege.

(3) INFORMATION FROM FEDERAL AGENCIES.—The Commission may secure directly from any Federal department or agency such information as the Commission considers necessary to carry out the provisions of this section. Upon request of the Commission, the head of such department or agency shall furnish such information to the Commission.

(4) HEARINGS.—The Commission may hold such hearings, sit and act at such times and places, take such testimony, and receive such evidence as the Commission considers advisable to carry out the objectives of this section, except that, to the extent possible, the Commission shall use existing data and research.

(5) POSTAL SERVICES.—The Commission may use the United States mails in the same manner and under the same conditions as other departments and agencies of the Federal Government.

(e) REPORT.—Not later than 1 year after all of the members are appointed to the Commission under subsection (c)(1), the Commission shall submit to Congress a report that summarizes the findings of the Commission and makes such recommendations for legislation as are consistent with this Act.

(f) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated to the Equal Employment Opportunity Commission such sums as may be necessary to carry out this section.

42 USC 2000ff–8.

SEC. 209. CONSTRUCTION.

(a) IN GENERAL.—Nothing in this title shall be construed to—

(1) limit the rights or protections of an individual under any other Federal or State statute that provides equal or greater protection to an individual than the rights or protections provided for under this title, including the protections of an individual under the Americans with Disabilities Act of 1990 (42 U.S.C. 12101 et seq.) (including coverage afforded to individuals under section 102 of such Act (42 U.S.C. 12112)), or under the Rehabilitation Act of 1973 (29 U.S.C. 701 et seq.);

(2)(A) limit the rights or protections of an individual to bring an action under this title against an employer, employment agency, labor organization, or joint labor-management committee for a violation of this title; or

Applicability.

(B) provide for enforcement of, or penalties for violation of, any requirement or prohibition applicable to any employer, employment agency, labor organization, or joint labor-management committee subject to enforcement for a violation under—

(i) the amendments made by title I of this Act;

(ii)(I) subsection (a) of section 701 of the Employee Retirement Income Security Act of 1974 as such section applies with respect to genetic information pursuant to subsection (b)(1)(B) of such section;

(II) section 702(a)(1)(F) of such Act; or

(III) section 702(b)(1) of such Act as such section applies with respect to genetic information as a health status-related factor;

(iii)(I) subsection (a) of section 2701 of the Public Health Service Act as such section applies with respect to genetic information pursuant to subsection (b)(1)(B) of such section;

(II) section 2702(a)(1)(F) of such Act; or

(III) section 2702(b)(1) of such Act as such section applies with respect to genetic information as a health status-related factor; or

(iv)(I) subsection (a) of section 9801 of the Internal Revenue Code of 1986 as such section applies with respect to genetic information pursuant to subsection (b)(1)(B) of such section;

(II) section 9802(a)(1)(F) of such Act; or

(III) section 9802(b)(1) of such Act as such section applies with respect to genetic information as a health status-related factor;

(3) apply to the Armed Forces Repository of Specimen Samples for the Identification of Remains;

(4) limit or expand the protections, rights, or obligations of employees or employers under applicable workers' compensation laws;

(5) limit the authority of a Federal department or agency to conduct or sponsor occupational or other health research that is conducted in compliance with the regulations contained in part 46 of title 45, Code of Federal Regulations (or any corresponding or similar regulation or rule);

(6) limit the statutory or regulatory authority of the Occupational Safety and Health Administration or the Mine Safety and Health Administration to promulgate or enforce workplace safety and health laws and regulations; or

(7) require any specific benefit for an employee or member or a family member of an employee or member under any group health plan or health insurance issuer offering group health insurance coverage in connection with a group health plan.

(b) GENETIC INFORMATION OF A FETUS OR EMBRYO.—Any reference in this title to genetic information concerning an individual or family member of an individual shall—

(1) with respect to such an individual or family member of an individual who is a pregnant woman, include genetic information of any fetus carried by such pregnant woman; and

(2) with respect to an individual or family member utilizing an assisted reproductive technology, include genetic information of any embryo legally held by the individual or family member.

(c) RELATION TO AUTHORITIES UNDER TITLE I.—With respect to a group health plan, or a health insurance issuer offering group health insurance coverage in connection with a group health plan, this title does not prohibit any activity of such plan or issuer that is authorized for the plan or issuer under any provision of law referred to in clauses (i) through (iv) of subsection (a)(2)(B).

42 USC 2000ff–9.

SEC. 210. MEDICAL INFORMATION THAT IS NOT GENETIC INFORMATION.

An employer, employment agency, labor organization, or joint labor-management committee shall not be considered to be in violation of this title based on the use, acquisition, or disclosure of medical information that is not genetic information about a manifested disease, disorder, or pathological condition of an employee or member, including a manifested disease, disorder, or pathological condition that has or may have a genetic basis.

Deadline. 42 USC 2000ff–10.

SEC. 211. REGULATIONS.

Not later than 1 year after the date of enactment of this title, the Commission shall issue final regulations to carry out this title.

42 USC 2000ff–11.

SEC. 212. AUTHORIZATION OF APPROPRIATIONS.

There are authorized to be appropriated such sums as may be necessary to carry out this title (except for section 208).

42 USC 2000ff note.

SEC. 213. EFFECTIVE DATE.

This title takes effect on the date that is 18 months after the date of enactment of this Act.

TITLE III—MISCELLANEOUS PROVISIONS

42 USC 2000ff note.

SEC. 301. SEVERABILITY.

If any provision of this Act, an amendment made by this Act, or the application of such provision or amendment to any person or circumstance is held to be unconstitutional, the remainder of this Act, the amendments made by this Act, and the application of such provisions to any person or circumstance shall not be affected thereby.

SEC. 302. CHILD LABOR PROTECTIONS.

(a) IN GENERAL.—Section 16(e) of the Fair Labor Standards Act of 1938 (29 U.S.C. 216(e)) is amended to read as follows:

Penalties.

"(e)(1)(A) Any person who violates the provisions of sections 12 or 13(c), relating to child labor, or any regulation issued pursuant to such sections, shall be subject to a civil penalty not to exceed—

"(i) $11,000 for each employee who was the subject of such a violation; or

"(ii) $50,000 with regard to each such violation that causes the death or serious injury of any employee under the age of 18 years, which penalty may be doubled where the violation is a repeated or willful violation.

"(B) For purposes of subparagraph (A), the term 'serious injury' means—

"(i) permanent loss or substantial impairment of one of the senses (sight, hearing, taste, smell, tactile sensation);

"(ii) permanent loss or substantial impairment of the function of a bodily member, organ, or mental faculty, including the loss of all or part of an arm, leg, foot, hand or other body part; or

"(iii) permanent paralysis or substantial impairment that causes loss of movement or mobility of an arm, leg, foot, hand or other body part.

"(2) Any person who repeatedly or willfully violates section 6 or 7, relating to wages, shall be subject to a civil penalty not to exceed $1,100 for each such violation.

"(3) In determining the amount of any penalty under this subsection, the appropriateness of such penalty to the size of the business of the person charged and the gravity of the violation shall be considered. The amount of any penalty under this subsection, when finally determined, may be—

"(A) deducted from any sums owing by the United States to the person charged;

"(B) recovered in a civil action brought by the Secretary in any court of competent jurisdiction, in which litigation the Secretary shall be represented by the Solicitor of Labor; or

"(C) ordered by the court, in an action brought for a violation of section 15(a)(4) or a repeated or willful violation of section 15(a)(2), to be paid to the Secretary.

"(4) Any administrative determination by the Secretary of the amount of any penalty under this subsection shall be final, unless within 15 days after receipt of notice thereof by certified mail the person charged with the violation takes exception to the determination that the violations for which the penalty is imposed occurred, in which event final determination of the penalty shall be made in an administrative proceeding after opportunity for hearing in accordance with section 554 of title 5, United States Code, and regulations to be promulgated by the Secretary.

Deadline.
Notification.
Regulations.

"(5) Except for civil penalties collected for violations of section 12, sums collected as penalties pursuant to this section shall be applied toward reimbursement of the costs of determining the violations and assessing and collecting such penalties, in accordance with the provision of section 2 of the Act entitled 'An Act to authorize the Department of Labor to make special statistical studies upon payment of the cost thereof and for other purposes' (29 U.S.C. 9a). Civil penalties collected for violations of section 12 shall be deposited in the general fund of the Treasury.".

29 USC 216 note.

(b) EFFECTIVE DATE.—The amendments made by this section shall take effect on the date of the enactment of this Act.

Approved May 21, 2008.

LEGISLATIVE HISTORY—H.R. 493 (S. 358):

HOUSE REPORTS: No. 110–28, Pt. 1 (Comm. on Education and Labor), Pt. 2 (Comm. on Ways and Means), and Pts. 3 and 4 (Comm. on Energy and Commerce).

SENATE REPORTS: No. 110–48 accompanying S. 358 (Comm. on Health, Education, Labor, and Pensions).

CONGRESSIONAL RECORD:

Vol. 153 (2007): Apr. 25, considered and passed House.

Vol. 154 (2008): Apr. 24, considered and passed Senate, amended.

May 1, House concurred in Senate amendment.

WEEKLY COMPILATION OF PRESIDENTIAL DOCUMENTS, Vol. 44 (2008):

May 21, Presidential remarks.

July 12, 2021 12:50 PM EDT Last Updated 3 months ago

Europe

Greece orders COVID-19 vaccinations as infections rise

Reuters 3 minute read

A woman waits after receiving a dose of the Moderna vaccine against the coronavirus disease (COVID-19) at

a newly opened vaccination centre in Athens, Greece, February 15, 2021. REUTERS/Alkis Konstantinidis

ATHENS, July 12 (Reuters) - Greece has made vaccinations against COVID-19 mandatory for certain workers and announced restrictions to contain the spread of the virus as infections have kept rising during the vital summer tourism season.

"The country will not shut down again because of some," Prime Minister Kyriakos Mitsotakis said in a televised address announcing the measures.

"It is not Greece that is in danger, but unvaccinated Greeks."

Nursing home staff will need to get vaccinated immediately, while healthcare workers will have to be vaccinated starting Sept. 1, Mitsotakis said.

As part of the new measures, only vaccinated customers will be allowed indoors in bars, cinemas, theatres and other closed spaces, he said.

A country of 11 million people, Greece has so far administered more than 5,200,000 first shots and about 41% of the general population is fully vaccinated, according to Marios Themistokleous, secretary-general in charge of vaccinations.

In an effort to entice more people to get vaccinated, the government has offered incentives including cash and free mobile data for youths to try to bring the rate up to 70% by autumn.

Greece's bio-ethics committee had recommended compulsory shots for health workers and staff at nursing homes "as a last resort measure" if efforts to encourage inoculation proved ineffective.

While there has been a debate around whether mandatory vaccinations are ethical, an opinion poll released by Skai television last week showed most Greeks favour the move for specific groups dealing with the public.

Greece will begin vaccinating teenagers aged 15 to 17 against the coronavirus this week, authorities said on Monday.

"The risk of illness in these ages is small, but real," said the head of Greece's vaccination committee, Maria Theodoridou.

"The main characteristic of this age group, however, is spreading the virus to their environment, which could include vulnerable or unvaccinated people."

Greece reported 2,065 new COVID-19 infections and 10 deaths on Monday, bringing the total number of infections since the pandemic began to 440,872 and the death toll to 12,802.

Reporting by Karolina Tagaris; Editing by David Clarke and David Gregorio

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Europe

Europe · 8:31 AM EDT

Putin's foes accuse Google and Apple of caving to Kremlin pressure

Russian opposition activists accused Alphabet's Google and Apple of caving to Kremlin pressure on Friday after the U.S. tech giants removed an anti-government tactical voting app from their stores on the first day of a parliamentary election.

Europe

EU unsure if women face higher risk of clots from AstraZeneca shot

7:32 AM EDT

Europe

Supply fears lead EU vaccine industry to seek home comforts

3:49 AM EDT

Europe

Albania votes in its first female dominated government

3:41 AM EDT

Europe

Australian PM says he made clear to France possibility of scrapping submarine deal

3:28 AM EDT

GUIDELINES FOR REGULATORY IMPACT ANALYSIS

2016

Office of the Assistant Secretary for Planning and Evaluation
U.S. Department of Health and Human Services

ACKNOWLEDGEMENTS

These *Guidelines for Regulatory Impact Analysis* were prepared for the U.S. Department of Health and Human Services (HHS) Analytics Team, under the leadership of Amber Jessup (Office of the Assistant Secretary for Planning and Evaluation). The primary authors were Lisa A. Robinson and James K. Hammitt (Harvard University Center for Risk Analysis and Center for Health Decision Science) and Jennifer R. Baxter (Industrial Economics, Incorporated, IEc). The work was performed between 2013 and 2016 under subcontract to IEc and Mathematica Policy Research; Ms. Baxter was the IEc Project Leader. Dr. Hammitt's work was also supported by an HHS Intergovernmental Personnel Act agreement. The authors were assisted by IEc staff including Lindsay Ludwig, who helped develop the initial drafts of several sections; Margaret Black, who provided additional editorial support and helped draft the related primer; and Michael Welsh, who helped develop the index and glossary.

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Acronyms

ASPE	Assistant Secretary for Planning and Evaluation
BLS	U.S. Bureau of Labor Statistics
CBO	Congressional Budget Office
CDC	Centers for Disease Control and Prevention
CEA	cost-effectiveness analysis
Census	U.S. Census Bureau
CPI	Consumer Price Index
CPS	Current Population Survey
CRA	Congressional Review Act
DOT	U.S. Department of Transportation
ECEC	Employer Costs for Employee Compensation
ECI	Employer Cost Index
EQ-5D	EuroQol-5 Dimensions
FDA	Food and Drug Administration
FICA	Federal Insurance Contributions Act
FRFA	Final Regulatory Flexibility Analysis
G&A	general and administrative
GAO	Government Accountability Office
GDP	gross domestic product
GSA	U.S. General Services Administration
HHS	U.S. Department of Health and Human Services
HRQL	health-related quality of life
HUI	Health Utilities Index
ICR	Information Collection Request
IRFA	Initial Regulatory Flexibility Analysis
IRS	Internal Revenue Service
NCS	National Compensation Survey
NHTSA	National Traffic Highway Safety Administration
O&M	operations and maintenance
OES	Occupational Employment Statistics
OMB	U.S. Office of Management and Budget
PRA	Paperwork Reduction Act
QALY	quality-adjusted life year
QCEW	Quarterly Census of Employment and Wages
QWB	Quality of Well-Being
RFA	Regulatory Flexibility Act
RIA	regulatory impact analysis
SBA	Small Business Administration
SBREFA	Small Business Regulatory Enforcement Fairness Act
SOP	standard operating procedure
UMRA	Unfunded Mandates Reform Act

VSL	value per statistical life
VSLY	value per statistical life year
WTA	willingness to accept compensation
WTP	willingness to pay

Chapter 1
Introduction

Executive Orders 12866 and 13563 (Clinton 1993, Obama 2011) call for a regulatory system that protects "public health, welfare, safety, and our environment while promoting economic growth, innovation, competitiveness, and job creation." To achieve these goals, the Department of Health and Human Services (HHS) analyzes the benefits, costs, and other impacts of significant proposed and final rulemakings, consistent with the requirements of the executive orders.

In the HHS 2011 *Plan for Retrospective Review of Existing Rules*, the Assistant Secretary for Planning and Evaluation (ASPE) was asked to establish an agency-wide Analytics Team to provide recommendations for strengthening regulatory analysis, leveraging the existing expertise of economists and analysts from throughout the Department's operating divisions.[1] The Analytics Team investigated current challenges and determined that guidance was needed to address common difficulties and to ensure consistent treatment across agencies. To meet that need, the Department developed these *Guidelines for Regulatory Impact Analysis* to assist its agencies in conducting economic analyses that meet the goals of the executive orders. This chapter briefly introduces related requirements and the contents of these *Guidelines*.

1.1 WHAT IS REGULATORY IMPACT ANALYSIS?

A regulatory impact analysis (RIA) reflects a well-established and widely-used approach for collecting, organizing, and analyzing data on the impacts of policy options, to promote evidence-based decision-making. It provides an objective, unbiased assessment that is an essential component of policy development, considering both quantifiable and unquantifiable impacts. Along with information on legal requirements, general policy goals, the distribution of the impacts, and other concerns, it forms the basis of the ultimate policy decision.

The RIA describes the effects of the regulation rather than advocating a particular approach. The arguments supporting the agency's decision are provided separately in the preamble to the *Federal Register* notice for the proposed and final regulation. The core of the RIA is an assessment of the benefits and costs of regulatory and other policy options in comparison to a "without regulation" (or "no action") baseline. In addition, the RIA includes supplementary analyses that respond to various statutory and administrative requirements.

WHY PREPARE AN RIA?

RIAs provide objective information and analysis that is essential for evidence-based decision-making. They include a benefit-cost analysis as well as other analyses mandated by various statutes and executive orders.

The RIA framework is described in general terms in Executive Orders 12866 and 13563 (Clinton 1993, Obama 2011).[2] More specific guidance and oversight is provided by the Office of Information and Regulatory Affairs within the U.S. Office of Management and Budget (OMB), which is part of the Executive Office of the President. OMB reviews both the regulation and the supporting analysis prior to promulgation.[3] Its primary analytic

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[1] We provide links to those documents that are freely available on the internet in the reference list. Where possible, we link to the webpage that features the document rather than to the document itself, so that readers can check for updates.

[2] These requirements apply only to the extent allowable by law.

[3] Under the Congressional Review Act (CRA), agencies must also submit final rules and supporting analyses to the Government Accountability Office (GAO) for congressional review prior to promulgation. This submission must indicate whether the rule is "major" as defined under the CRA (5 USC §804(2)): "'major rule' means any rule that the Administrator of the Office of Information and Regulatory Affairs of the Office of Management and Budget finds has resulted in or is likely to result in — (A) an annual effect on the economy of $100,000,000 or more; (B) a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or (C) significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic and export markets. The term does not include any rule promulgated under the Telecommunications Act of 1996 and the amendments made by that Act." More information is available on the GAO website (http://www.gao.gov/legal/congressact/cra_faq.html).

guidance is provided in *Circular A-4* (2003); it summarizes related requirements in a checklist for agencies (2010), a compilation of frequently-asked questions (2011a), and a primer (2011b). The OMB checklist is replicated in Appendix A of this document. Examples of RIAs completed by HHS and other agencies can be found by searching regulations.gov; however, analysts should be aware that many of the HHS analyses were completed prior to issuance of these *Guidelines*.[4]

In addition to the assessment of the benefits and costs, the RIA may include supplementary analyses that address the following, as relevant.

- the distribution of the impacts;
- the Unfunded Mandates Reform Act;
- the Regulatory Flexibility Act and Small Business Regulatory Enforcement Fairness Act;
- Executive Order 13132, "Federalism;"
- Section 1102(b) of the Social Security Act, small rural hospitals; and,
- the Paperwork Reduction Act.

More information on these requirements, as well as on the conduct of the benefit-cost analysis, is provided in the subsequent chapters of this guidance.

1.2 WHAT ARE THE BENEFITS AND COSTS OF CONDUCTING AN RIA?

The most important goals of the RIA are (1) to indicate whether Federal regulation is necessary and justified, and, if so, (2) to identify the regulatory option that is most economically efficient, providing the largest net benefits to society. A well-conducted RIA has numerous additional benefits. It develops the evidence to support well-informed decision-making and supplies a record of the data, assumptions, and analyses considered – providing a reasonable basis for rulemaking as required by the Administrative Procedures Act.

The RIA plays several other useful roles. For example, it:

- encourages comprehensive consideration of impacts;
- provides information on important regulatory outcomes expressed in physical and behavioral terms;
- estimates the economic value of the outcomes, based on the preferences of those who are affected;
- anticipates potential side effects, beneficial and adverse;
- supports consideration of non-quantifiable effects and uncertainty; and,
- aids decision-makers and stakeholders in clarifying areas of agreement and disagreement.

The costs of conducting RIAs include the need to devote staff and funding to preparing these assessments rather than to other tasks. To ensure the efficient use of these resources, the analysis should be carefully tailored to focus on providing the information that is most important for decision-making. Screening analysis, discussed in the following chapter, is a useful tool for targeting efforts.

1.3 WHEN IS AN RIA REQUIRED?

An RIA is required for significant and economically significant regulatory actions as defined under Executive Order 12866 (§3(d-f)) and Executive Order 13563. An economically significant regulatory action is one that:

- is likely to **impose costs, benefits, or transfers of $100 million or more** in any given year, or
- "adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities" (Clinton 1993, §3(f)(1)).

[4] Many agencies also post their RIAs on their websites. For example, analyses completed by the Food and Drug Administration (FDA) can be found at: http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm.

If a regulation is economically significant, then the analysis discussed in OMB *Circular A-4* (and described in more detail in these *Guidelines*) must be completed (Clinton 1993, §6(a)(3)(C)).

In addition, many other regulations are considered "significant," defined as those that:

- "[c]reate a serious inconsistency or otherwise interfere with an action taken or planned by another agency;
- [m]aterially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or
- [r]aise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive order" (Clinton 1993, §3(f)(2-4)).

For regulatory actions that are significant, but not economically significant, Executive Order 12866 requires:

- "a reasonably detailed description of the need for the regulatory action and an explanation of how the regulatory action will meet that need," and
- "[a]n assessment of the potential costs and benefits of the regulatory action" (Clinton 1993, §6(a)(3)(B)).

HOW DOES OMB INTERPRET THE $100 MILLION THRESHOLD?

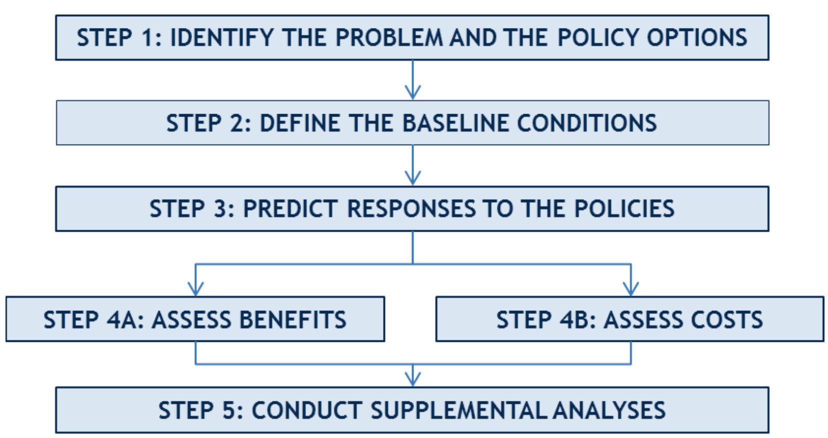
An RIA is required for economically significant regulations. In defining "economically significant," OMB (2011a) states, "The $100 million threshold applies to the impact of the proposed or final regulation in any one year, and it includes benefits, costs or transfers." The word "or" is important: the categories are considered separately, not summed, so $100 million in any of the three categories -- annual benefits, or costs, or transfers -- is sufficient. For example, a regulation with $75 million in benefits, $60 million in costs, and $40 million in transfers is not economically significant. An RIA is also required for regulations deemed to be significant for other reasons and is an essential element of good regulatory practice.

Agencies may wish to complete RIAs for regulations that are not defined as significant to improve the foundation for decision-making and to demonstrate the rationale and basis for the action.

1.4 WHAT ARE THE BASIC COMPONENTS?

The remaining chapters of this guidance are organized around the major components of an RIA, as illustrated in Figure 1.1.

FIGURE 1.1. MAJOR RIA COMPONENTS



- The first three steps are discussed in **Chapter 2: Frame the Analysis**.
- Steps 4A and 4B are described in detail in **Chapter 3: Assess Benefits** and **Chapter 4: Assess Costs**.
- Topics that affect the assessment of both benefits and costs are considered in **Chapter 5: Account for Timing** and **Chapter 6: Address Uncertainty and Nonquantifiable Effects**.
- The analyses under step 5 are discussed in **Chapter 7: Conduct Distributional and Other Supplementary Analyses.**
- The presentation of the results is considered in **Chapter 8: Communicate the Approach and Results.**
- The *Guidelines* conclude by turning from the discussion of *ex ante* (prospective) analysis to *ex post* analysis in **Chapter 9: Conduct Retrospective Analysis.**

Supplementary information is provided in the appendices.

Chapter 2

Frame the Analysis

Conducting an RIA involves first defining the problem to be addressed, identifying the policies to be assessed, exploring their potential consequences, and developing the approach for subsequent analytic work. This chapter describes these steps, focusing on the benefit-cost analysis that forms the core of the RIA. As introduced in Chapter 1 and discussed in more detail in Chapter 7, an RIA includes several supplementary analyses, to which the principles discussed in this chapter also apply. These analyses should be initiated in the early stages of the regulatory development process, to inform both internal agency deliberations and discussions with other stakeholders.

Benefit-cost analysis is a well-established systematic framework, based on economic welfare theory, for assessing and comparing the positive and negative impacts of policy options. It addresses the question of whether those affected by the policy, in the aggregate, value the benefits they receive more than the costs they incur. The distribution of the impacts (who receives the benefits and who bears the costs) is assessed separately (see Chapter 7).

The goal of the benefit-cost analysis is to indicate how limited resources can be best allocated to maximize net social welfare. Welfare is based on individual preferences, and money is used as a convenient and practical numeraire (or measuring rod) that describes the extent to which individuals are willing, as a society, to reduce their consumption of other goods and services to achieve the policy outcomes.

Conducting a benefit-cost analysis is often useful and informative even if the resulting summary measure – net benefits (benefits minus costs, which may be positive or negative) – is not used as a decision-making criterion or is only one of many factors considered.[5] The data and analysis provide a wealth of information on possible impacts, including many that often were not anticipated or predicted, and this information has important implications for regulatory design and implementation. The analysis should be descriptive, providing unbiased and objective information.

Framing the analysis involves defining what will be assessed and developing the general analytic approach. This chapter describes related activities, including explaining the need for the action and identifying the alternatives to be addressed, specifying the baseline, and determining the consequences of the regulation. It concludes by describing how screening analysis can be used to target analytic resources.

2.1 EXPLAIN THE NEED FOR ACTION AND IDENTIFY ALTERNATIVES

Consistent with OMB *Circular A-4*, agencies must first describe the market failure or other social purpose that leads to the need for regulatory action. They must also describe why action at the Federal level, rather than at the State or local level, is necessary or desirable. Agencies must indicate the significance of the regulation, based on the definitions in Executive Order 12866 that are replicated in the previous chapter.

[5] The normative basis for using benefit-cost analysis in decision-making begins with the Pareto principle, which states that a policy is desirable if it makes at least one person better off and no one worse off. While attractive in theory, few policies meet this criterion: most will harm (or impose costs on) at least a few people. To address this limitation, variations were developed by Nicholas Kaldor and John Hicks. These variations state that a policy is desirable if it makes the winners better off by an amount large enough to compensate the losers, and, alternatively, that it should be rejected if the losers could compensate the winners to not pursue the policy. These criteria do not demand that actual compensation take place. They imply that a policy for which costs exceed benefits should not be adopted and, if more than one policy provides positive net benefits, the one with the largest net benefits should be adopted. This principle is rarely applied strictly, as regulatory and other policy decisions are based on several considerations in addition to the results of the benefit-cost analysis.

Agencies must also consider a range of regulatory and non-regulatory alternatives, regardless of whether the statute or other authorities prescribe the option they can ultimately implement.[6] OMB *Circular A-4* lists the types of alternatives that should be considered, not all of which will be applicable to a particular regulation:

- different choices defined by statute;
- different compliance dates;
- different enforcement methods;
- different degrees of stringency;
- different requirements for different sized firms;
- different requirements for different geographic areas;
- performance standards rather than design standards;
- market-oriented approaches rather than direct controls; and,
- informational measures rather than regulation.[7]

HOW MANY ALTERNATIVES MUST BE ANALYZED?

Agencies must justify the need for regulatory action and consider a range of policy alternatives. These alternatives must, at minimum, include at least one that is more stringent and one that is less stringent than the preferred option; additional options should also be assessed.

Considering a wide-range of options both helps inform agency decision-making and encourages public comment. The versions of the analysis published to support the proposed and the final rule must include, at the very least, comprehensive analysis of one option that is more stringent and one that is less stringent than the preferred option; in total, more than three options should be assessed. These options should represent diverse approaches to meeting the policy goals and should be sufficiently distinct for the analysis to differentiate among them. In some cases, the statute or other legal constraints, or issues of technical feasibility, will limit the types of alternatives considered; this should be explicitly noted in the RIA. However, an option does not need to be legally permissible to be assessed.

Prior to promulgation, the analysis conducted to support the regulatory development process should consider a substantially broader array of options, which may be subject to varying degrees of assessment depending on their feasibility and likely impacts. These additional options also should be discussed in the RIA documentation to encourage public review and comment.

Selecting alternatives for assessment is an iterative process. As analysts gain a better understanding of the benefits and costs of the options, the alternatives to be included in the final RIA are likely to be altered and refined. Screening analysis, discussed later, can be used to eliminate many alternatives from detailed consideration. The rationale for excluding and including alternatives, and the alternatives excluded, should be explicitly discussed when documenting the analysis.

2.2 DEFINE THE "WITHOUT REGULATION" BASELINE

Each regulatory and non-regulatory alternative must be compared to a "no new regulatory action" baseline that reflects expected future conditions.[8] The analysis should, at minimum, compare conditions with and without the policy once the policy is fully implemented. This may occur several years from the present, given the time needed for notice and comment as well as implementation. In many cases, benefits and costs that accrue over the transition period may be significant and should be assessed. In some cases, there may be a significant time lag between when costs are incurred and when benefits accrue or vice-versa. In such cases, the analysis should cover the full time period between when the impacts first occur and when benefits and costs are expected to

[6] RIAs also aid the agency in identifying ways in which the statute can be improved. OMB *Circular A-4* notes: "You should also discuss the statutory requirements that affect the selection of regulatory approaches. If legal constraints prevent the selection of a regulatory action that best satisfies the philosophy and principles of Executive Order 12866, you should identify these constraints and estimate their opportunity cost." (OMB 2003, p. 17)

[7] Alternatives that provide information and disclosure are discussed in more detail in Sunstein (2010a).

[8] If the regulation is required by statute, the baseline should reflect the absence of the statutory requirement.

achieve equilibrium.[9] The RIA should generally consider benefits and costs that accrue over a 10 to 20 year time period, unless the program is expected to end sooner.

Analysts should explore likely trends rather than simply assuming that current conditions will continue. These projections should address future economic and health conditions as well as other factors that may affect the regulatory environment. Where future conditions are uncertain and changes in baseline assumptions significantly affect the analytic results, analysts should consider modeling more than one baseline or testing the sensitivity of their results to key assumptions.

WHAT IS THE APPROPRIATE TIMEFRAME FOR THE ANALYSIS?

In theory, the timeframe for the analysis should begin when regulated entities or others begin to change their behavior in response to the regulation (which may occur before or after the effective date of the regulation) and end when the impacts of the regulation cease. However, it is generally difficult to reasonably forecast effects far into the future. OMB suggests that if the proposed regulation has no predetermined sunset provision, the agency should use its best judgment about the foreseeable future. "For most agencies, a standard time period of analysis is 10 to 20 years, and rarely exceeds 50 years" (OMB 2011a).

Any difference between the baseline and a policy alternative may have both positive and negative consequences, and both should be considered. Conversely, neither the costs nor the benefits of changes predicted in the absence of the regulation should be attributed to the rule. For example, if a change in food handling procedures is expected under the baseline, the associated costs would not be counted as costs of the regulation. Similarly, the benefits of that change would have materialized in the baseline and cannot be attributed to the regulation.

When developing the baseline, analysts should also consider who has "standing;" i.e., whose benefits and costs should be counted. OMB *Circular A-4* (2003) indicates that the analysis should focus on U.S. residents and citizens. At times, determining standing raises difficult issues, such as how to address the preferences of those engaged in illegal activities. When such issues arise, the analysts should explicitly discuss their treatment in the RIA documentation.

If a regulation is likely to have impacts outside of the United States, these impacts should be assessed separately (see Chapter 7). A related issue is whether to assess only the immediate or direct impacts of the regulations, or to also account for second-order or indirect effects, which may affect different groups of people. Screening analysis is a useful tool for determining whether these less immediate effects are significant enough that they should be considered.

2.3 DESCRIBE THE CONSEQUENCES OF EACH POLICY ALTERNATIVE

One of the most difficult steps in conducting regulatory analysis is predicting responses to the policy options, given an evolving baseline, complex regulatory requirements, data gaps, and the diversity of the individuals and organizations affected. Regulatory requirements typically lead to a series of consequences (events and outcomes). It is important to distinguish between the initial requirement (e.g., hospitals must report certain adverse drug reactions); subsequent events (e.g., hospital staff change their prescribing behavior); the ultimate outcome (e.g., greater health improvements for some patients in comparison to the baseline); and its evaluation (e.g., the monetary value of the behavioral changes and the health improvements). Evidence must be used to establish the causal link between these events and outcomes. Analysts often find it useful to map these relationships as a decision tree (Raiffa 1968) or as a logic model (Centers for Disease Control and Prevention (CDC) 2007, Sundra et al. 2003, Wholey et al. 2010), which can be updated as more is learned about likely impacts.

[9] For meaningful comparison, benefits and costs should be measured over the same time period. If the nature of the impacts is such that assessing some over longer periods than others provides important information, the time period over which only some impacts are assessed should be reported separately when summarizing the analysis to avoid misleading comparisons.

Whether a particular consequence is classified as a benefit or cost does not affect the estimated net benefits, as long as the sign is correct (i.e., positive benefits and negative costs increase net benefits; negative benefits and positive costs decrease net benefits).[10] However, for clear communication, analysts should follow a consistent approach. Impacts categorized as benefits should relate to the intended outcome of the regulation (e.g., improved health); impacts categorized as costs should relate to the investment or inputs needed to achieve those outcomes (e.g., safety expenditures by industry). In this case, any negative effects that relate to the intended outcomes (e.g., through substitution of less safe drugs or less healthy foods for those that are regulated) would be combined with the benefit estimates, while any offsetting savings from regulatory compliance (e.g., increased efficiency from automation of previously manual tasks) would be combined with the cost estimates.

WHEN SHOULD AN IMPACT BE CLASSIFIED AS A COST VERSUS A BENEFIT?

Costs are the inputs needed to implement the regulation (e.g., industry expenditures to improve safety); benefits are the intended outcomes (e.g., health improvements). Counterbalancing effects, such as cost-savings (e.g., lower operating costs if the regulation allows industry to replace older technology with more efficient equipment) or negative benefits (e.g., health risks of substituting less safe drugs or less healthy foods) should be assigned to the same category as the effect they offset; i.e., as costs and benefits respectively.

Understanding these consequences is an iterative process, as each step in the analysis often provides new insights. Initially, analysts should describe the possible outcomes ("fewer cases of cardiac and respiratory disease," "higher production costs") in as much detail as possible. What is ultimately assessed and quantified, and the level of detail, will depend on the results of the subsequent screening, as well as on what is learned in the course of the analysis.

Analysts should comprehensively consider all potentially important consequences, including both those that are intended and unintended (positive or negative). They should also consider whether behavioral anomalies will lead to different outcomes than expected under the rational actor model typically assumed in economics. For example, individuals may respond to policies intended to increase safety by reducing their level of precaution, or such polices may lead to changes in social norms that lead to healthier behaviors. Another example is hyperbolic discounting (or present bias, sometimes described as self-control problems), which can lead individuals to engage in behavior (such as eating too much, exercising too little, or continuing to smoke) that is contrary to their own self-described preferences.[11]

Evaluating these consequences, through estimating their monetary value, is discussed in Chapters 3 and 4. These monetary values should be estimated as accurately and comprehensively possible, given analytic goals and time and resource constraints. Effects that cannot be quantified should be highlighted for consideration by decision-makers, as described in Chapter 6. That chapter also discusses methods for addressing uncertainty in the quantitative results.

2.4 USE SCREENING TO FOCUS THE ANALYSIS

Once the initial framing of the analysis is completed, as discussed above, the subsequent steps involve determining how to best target future work, conducting the analysis, and reporting the results, as illustrated in Figure 2.1. Analysts will need to follow a similar process to determine the types of supplemental analyses to be conducted and the focus of that work. These processes are iterative; each step in the analysis will result in another round of decisions about whether to address certain impacts in more detail or focus attention elsewhere.

[10] Whether an impact is counted as a benefit or cost will affect the ratio of benefits to costs. As noted in OMB *Circular A-4*, benefit-cost ratios (and cost-benefit ratios) can be misleading (OMB 2003, p. 10) and generally should not be used as an indicator of economic efficiency. To avoid misunderstanding, such ratios should not be reported unless accompanied by information clarifying their appropriate interpretation.

[11] For more discussion of the valuation of the benefits of HHS policies that address habitual or addictive goods, see Cutler et al. (2015).

FIGURE 2.1. ANALYTIC STEPS

DEVELOP THE ANALYTIC FRAMEWORK

Define the problem to be addressed. Identify the policy options to be considered; the costs and benefits to be assessed; and the geographic areas, types of industry and other entities, and population groups to be considered. Explore the extent to which quantitative analysis is practicable.

↓

CONDUCT SCREENING ANALYSIS

Use available information and simple assumptions to provide preliminary information on the direction and magnitude of effects, to identify the extent to which more research is justified, and to focus future work.

↓

CONDUCT DETAILED ANALYSIS

Estimate the magnitude and economic value of important consequences, compare costs and benefits, and address uncertainty. Refine the approach as needed and complete the analysis.

↓

REPORT THE RESULTS, ADDRESSING NONQUANTIFIED IMPACTS AND OTHER UNCERTAINTIES

Present findings in text and in tables and graphics.

Screening analysis is a useful tool for targeting subsequent work. Such analysis is typically based on easily accessible data and simple assumptions; its goal is to provide preliminary information on the possible direction and magnitude of the effects and to inform decisions about future work. For example, high-end values can be used to determine whether various types of outcomes are likely to be significant even under extreme assumptions. Depending on the results, this screening may be followed by more detailed assessment that involves collecting additional data, refining the methods used, and possibly expanding the scope of the analysis as discussed in the following chapters. The analysis should discuss non-quantified impacts along with the quantitative results, and include assessment of uncertainties. The RIA should clearly document the results, as well as discuss the data sources and analytic steps and the implications of uncertainties.

Because analytic resources are limited, the ideal regulatory analysis will not assess all policy options, nor quantify all outcomes, with equal precision. In some cases, the cost of analyzing a particular policy option or quantifying a specific outcome will be greater than the likely benefit of assessing it, given its importance for decision-making.[12] In other words, the analysis may not sufficiently improve the basis for decision-making to pass an informal benefit-cost or value-of-information test. Conversely, options and outcomes that are important for decision-making should receive substantial attention. "Importance" may depend on the likely magnitude of the impacts; it may also depend on the need to respond to questions likely to be raised by decision-makers and others.

The content and level of detail, and the length of the RIA (which may be very short or very long), are likely to depend on the nature of the regulation, the characteristics of its benefits and costs, the populations affected, and the data and other analytic resources available. It is not possible to design a "one size fits all" approach; analysts need to exercise professional judgment in tailoring the analysis for an individual regulation. Generally, conducting screening analysis and following a phased approach will help ensure that the work is carefully focused and useful.

[12] Such decisions include those related to assessing whether statutory change may be desirable; as noted earlier, the analysis need not be limited to considering options allowed under current law.

Chapter 3
Assess Benefits

HHS regulations have many beneficial outcomes, including cost-savings as well as reduced health risks. As introduced in Chapter 2, the distinction between benefits and costs is not always clear. Generally, impacts categorized as benefits should relate to the intended outcomes of the regulation; i.e., the welfare improvements that comprise its goals. Impacts categorized as costs should relate to the investment or inputs needed to achieve those outcomes.

Methods for assessing both increases and decreases in costs are discussed in Chapter 4; this chapter addresses changes in health risks.[13] Such benefits are often the primary goal of HHS regulations and generally cannot be valued using market measures.[14] Calculating these benefits requires first estimating the change in risk associated with each regulatory and non-regulatory option (in comparison to the baseline) then estimating its monetary value. Below, we focus on valuation, first introducing basic concepts and methods, then describing specific approaches for application in HHS analyses.

3.1 BASIC CONCEPTS

The starting point for valuation is an estimate of the impact of each regulatory option on specific health effects, generally expressed as a change in the probability of illness or death for the average affected individual. The monetary value of the benefit to the average individual can be calculated as the change in probability of the illness or death multiplied by the value per statistical case, and summed across the affected population.

In practice, there is often little information on how the risk reduction or the value per statistical case varies across individuals. It is common practice to aggregate the changes in risk over the affected population to calculate the number of "statistical" cases averted by a regulation or other policy, and to multiply this by an average value per statistical case.[15] If, for example, a regulation would decrease the individual risk of a particular illness or death by 10/20,000 annually throughout a population of 200,000, then 100 statistical cases would be averted each year. The calculation is straightforward:

10/20,000 risk reduction x 200,000 individuals annually

= 100 statistical cases

Thus averting a statistical case or "saving" a statistical life is not the same as preventing an identifiable individual from becoming ill or dying; rather, it is a sum of probabilities.[16]

The question for the regulatory analyst is thus how to best estimate the value of these risk changes. Because we currently lack high quality, applicable studies that can be used to value the combined risk of illness and death, we generally estimate the number of averted statistical cases of premature mortality and of morbidity separately, then apply values to each and sum the results. The framework and methods for estimating these values is described below.

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[13] Information on valuing other types of benefits, such as environmental improvements, is available in the U.S. Environmental Protection Agency's *Guidelines for Preparing Economic Analysis* (2014) and in Freeman et al. (2014).

[14] The goal of some regulations is to provide cost-savings rather than risk reductions. In such cases, these savings would be categorized as benefits and the methods described in the cost chapter would be used to value them. At times, whether to include an impact as a benefit or cost will be unclear, and analysts will need to document this uncertainty in describing how the impact is categorized in the RIA.

[15] This second approach yields the same result as the first, theoretically correct, approach if the risk reduction is the same across individuals, or the value per statistical case is the same across individuals, or the risk reduction and value per statistical case are uncorrelated in the population.

[16] In is typically impossible to identify *ex ante* whose illness or death will be prevented by a rule; in many cases, it is also impossible *ex post*.

3.1.1 ECONOMIC FOUNDATION

The approach for valuing mortality and morbidity risk reductions, as well as other policy impacts, is grounded in four basic assumptions that underlie the standard economic model. The first is that each individual is the best judge of his or her own welfare. This principle of consumer sovereignty means that benefit values should be based on the preferences of those affected by a policy. Such framing allows analysts to provide decision-makers with information on how those who would benefit are likely to value the improvement in their own health or longevity.

The second is that individuals can be modeled as deriving utility (well-being) from the goods and services they consume. If an individual chooses to buy a good or service, economists conventionally assume (consistent with consumer sovereignty) that he or she values the good or service more than the other goods or services he or she could have used that money to buy. Thus an individual's willingness to exchange money for different goods and services can be used to measure the utility he or she receives from their consumption. The monetary value of a risk reduction is appropriately measured by determining the change in wealth that has the same effect on utility as the risk reduction.

The third is that estimates of individual willingness to pay (WTP) provide a conceptually appropriate measure of value.[17] WTP is the maximum amount of money an individual would voluntarily exchange to obtain an improvement, given his or her budget constraints. It indicates the point at which the individual would be equally satisfied with having the good and less money, or with spending the money on other things. In addition to reflecting the trade-offs individuals make in everyday decisions related to spending on health and safety, this framing mimics the actual trade-offs implicit in regulation. If we as a nation choose to spend more, for example, on regulations that reduce food pathogen risks, we will have less to spend on other goods or services – including other risk-reducing measures.

The fourth key assumption is that benefit values are determined by the change in the amount by which aggregate WTP exceeds the market price, or "consumer surplus." When WTP exceeds price, the individual benefits from the fact that he or she can acquire the good or service for less than his or her willingness to pay. If price exceeds WTP, the individual would not purchase the good or service. The difference between WTP and price can be aggregated across individuals to determine the consumer surplus associated with different price levels. Consumers generally benefit from price decreases, because WTP then exceeds price by a larger amount, and vice-versa. More information on this concept is provided in Appendix B.[18]

WHAT IS THE BASIS FOR VALUATION?

Benefits are valued based on the maximum amount of money an individual would willingly exchange for the improvement, reducing his or her ability to purchase other things. This means that the value of mortality and morbidity risk reductions is determined by the affected individuals' willingness to pay for the change in their own risk.

3.1.2 VALUATION METHODS

For goods such as mortality and morbidity risk reductions, prices do not exist because they are not directly bought and sold in markets. Instead, we use the methods described below to estimate how much individuals would be willing to pay for the risk reductions. We can then compare aggregated WTP for these risk reductions (and other benefits) to the costs of a policy to determine the extent to which it is likely to yield net benefits.

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[17] Estimates of willingness to accept compensation (WTA); i.e., of the least amount of money an individual would accept to forgo an improvement, are also consistent with this framework (see Robinson and Hammitt 2011, 2013). We refer to WTP throughout this discussion because it is more frequently studied. In addition, regulations generally involve spending for improvements from the status quo, rather than compensation to forego an improvement, in which case WTP is conceptually more appropriate.

[18] A similar concept applies to producers, who earn a surplus when they can supply units of a good for less than the market price, as discussed in Appendix B.

For nonmarket outcomes, economists typically rely on revealed or stated preference studies to estimate WTP.[19] Each has advantages and limitations: the choice of approach depends on the quality of the available research and the extent to which it measures an outcome similar to the policy outcome.

Revealed preference studies rely on observed market behavior to estimate the value of related nonmarket goods. For example, wage-risk (hedonic-wage) studies examine the compensation associated with jobs that involve differing risks of death or nonfatal injury, using statistical methods to separate the effects of these risks from the effects of other job and personal characteristics. While such methods have the advantage of relying on actual behavior with real consequences, it may be difficult to find a market good that can be used to estimate the value of a particular policy outcome.

Stated preference methods typically employ survey techniques to ask respondents about their WTP for the outcome of concern. Such surveys may directly elicit WTP for a particular scenario, or may present respondents with two or more scenarios involving different attributes and prices.[20] In the latter case, estimates of WTP are derived from the way in which respondents choose, rank, or rate alternatives. Stated preference methods are attractive because researchers can tailor them to directly value the outcomes of concern; for example, the survey can describe a particular type of illness from a particular type of exposure. A potential weakness is that respondents do not directly experience the consequences of their decisions and may have limited incentives to consider the questions carefully. Such surveys must be carefully designed and administered and satisfy various tests for coherence to be considered reliable for use in regulatory analysis.

Analysts often must rely on existing studies when estimating parameters values as well as their interrelationships, due to the substantial time and expense associated with conducting new primary research. When used to value benefits, this approach is typically referred to as “benefit transfer,” and generally consists of the five steps described in Figure 3.1. It requires careful review of the literature to identify high-quality studies that are suitable for use in a particular context. “Quality” can be evaluated by considering the likely accuracy and reliability of the data and methods used, referencing guidance on best practices.[21] “Suitability” or “applicability” involves considering the similarity of the risks and the populations affected.

In the subsequent sections, we describe how this framework should be used by HHS regulatory analysts to value mortality and morbidity risk reductions. Numerous studies of the value of mortality risk reductions have been conducted; morbidity risk reductions have received substantially less attention. In the latter case, because fewer studies have been completed, analysts often rely on proxy measures.

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[19] Experimental methods (see, for example, Shogren 2005) and structural models that combine theoretical expectations with data from various sources (see, for example, Smith et al. 2006) are less frequently applied but may be useful in some cases.

[20] Although the terminology is not always used consistently, the first type of study is usually referred to as a contingent valuation survey; the second as a choice experiment.

[21] Some guidelines for determining study quality are provided in OMB (2003) and EPA (2014) as well as in the sources cited in this guidance. Because these methods are continually evolving as additional research provides new insights, analysts should also consult recent articles and reports for updated guidance.

FIGURE 3.1. BENEFIT TRANSFER FRAMEWORK

(1) DESCRIBE THE POLICY OUTCOME

Determine the characteristics of the risks and populations to be addressed by the policy options.

(2) IDENTIFY POTENTIALLY RELEVANT EXISTING VALUATION RESEARCH

Search the valuation literature for primary research studies that address similar risks and populations.

(3) REVIEW EXISTING STUDIES FOR QUALITY AND APPLICABILITY

(a) Assess the quality of the data and methods used in the primary research studies, considering the extent to which they follow generally accepted best practices and provide evidence of validity and reliability.

(b) Assess the applicability of the studies to the policy outcome including: (i) the similarity of the health risks; (ii) the similarity of the populations experiencing the risks; and (iii) the ability to adjust for differences between the scenario studied and the policy scenario.

(4) TRANSFER THE ESTIMATE(S)

Conduct the transfer, making any necessary adjustments to the primary research estimates and applying them to the policy outcome. Depending on the research available, this transfer may rely on a single study or combine the results from several studies, and may involve transferring a point estimate or a valuation function that tailors the estimate to the policy outcome.

(5) ADDRESS UNCERTAINTY

Assess uncertainties in the estimates both qualitatively and quantitatively; e.g., by conducting sensitivity or probabilistic analysis and discussing the implications for decision-making.

3.2 VALUING MORTALITY RISK REDUCTIONS

The approach for valuing mortality risk reductions is generally based on estimates of the value per statistical life (VSL), from which a value per statistical life year (VSLY) is sometimes derived.[22] We first introduce both concepts then discuss recommendations for HHS analyses.

3.2.1 THE VALUE PER STATISTICAL LIFE AND THE VALUE PER STATISTICAL LIFE YEAR

As noted earlier, the starting point for valuation is typically an estimate of the individual risk change associated with each regulatory option. Valuation also starts at the individual level, estimating what an individual would be willing to pay for a defined change in his or her own risk, consistent with the principle of consumer sovereignty. Values for mortality risk reduction reflect the rate of tradeoff between money and small changes in mortality risk, referred to as the marginal rate of substitution between wealth and risk (Hammitt 2000). This value is conventionally reported in dollars per statistical life (the VSL), and often estimated by dividing the value of a small risk reduction by the size of the risk change.[23] For example, if an individual is willing to pay $900 for a 1 in 10,000 reduction in his or her risk of dying in the current year, his or her VSL is calculated as:

$900 WTP ÷ 1/10,000 risk change

= $9.0 million VSL

[22] Recommendations related to the use of the VSL or VSLY in HHS RIAs are discussed later in this chapter.

[23] For the U.S. population, the annual likelihood of dying at each year of age increases from about 10/10,000 to about 100/10,000 between age 20 and age 65, conditional on surviving to that age (Arias 2014).

The key parameter is the individual's WTP for the 1 in 10,000 risk reduction (i.e., the $900); it is expressed as the VSL (i.e., the $9.0 million) largely for convenience.[24] The value of a *statistical* life is not the value of saving an individual's life with certainty.

In principle, WTP should change nearly in proportion to the change in risk, as long as the risk change is small enough that WTP does not substantially limit other spending. Thus a single VSL can be used to value a range of small risk changes.[25] In other words, if we decrease the risk change in the above equation by a factor of 10, to 1/100,000, we assume that WTP will also decrease by a factor of 10, so the VSL will still be $9.0 million (= $90 WTP ÷ 1/100,000 risk change).

The VSLY is a related concept. In contrast to the VSL, which is the rate at which the individual substitutes money for reductions in current mortality risk (within the current year or other short time period), the VSLY is the rate at which he or she substitutes money for gains in life expectancy. A reduction in current mortality risk implies a corresponding increase in life expectancy and hence a corresponding gain in life years.[26]

Under the VSLY approach, a reduction in mortality risk is typically valued by calculating the corresponding gain in life expectancy and multiplying it by a VSLY. (Generally, future life years are first discounted to account for time preferences; discounting is discussed in more detail in Chapter 5.) As does WTP more generally, both the VSLY and the VSL vary depending on the characteristics of the individual and of the risk, and may increase, decrease, or remain the same depending on the age (and remaining life expectancy) of the affected individual. However, few primary research studies directly estimate the VSLY; it is typically instead derived from a VSL estimate using simple assumptions.

3.2.2 LITERATURE REVIEW

HHS commissioned a review of the VSL literature to identify values that are suitable for use in its regulatory analyses (Robinson and Hammitt 2016). The review had two goals: (1) to identify studies that meet evolving criteria for "best practices" for VSL research; and (2) to tailor the estimates used by HHS to the types of risks it regulates.

The criteria for that review were derived from several reports and articles that describe best practices for valuing mortality risk reductions in regulatory analyses (OMB 2003, EPA 2010, Kling et al. 2011, Cropper, Hammitt, and Robinson 2011, and U.S. Department of Transportation (DOT) 2015a). The criteria are listed in Figure 3.2 and discussed in more detail by Robinson and Hammitt (2016) as well as in these source documents.

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[24] The VSL is at times described as aggregating individual WTP across a population; i.e., if each individual is willing to pay $900 for a 1 in 10,000 risk, and the population included 10,000 such individuals, then the value per statistical case would be $9 million ($900 * 10,000 individuals). This definition can be misleading, however, because WTP for a similar risk reduction is likely to vary across individuals.

[25] Many VSL studies consider risks in the range of 1/10,000 or 1/100,000. While applying the resulting VSL to smaller risk changes is appropriate, care must be taken in cases where the risk change is substantially larger. As the risk change increases, WTP will be increasingly limited by income, reducing the VSL (see Alolayan et al. 2015 for more discussion).

[26] Because death can be postponed but not prevented, reducing the risk of dying at one time necessarily increases the risk of dying at some later time. Similarly, reducing the chance of dying from one cause necessarily increases the risk of dying from some other cause. For example, if a policy were to reduce the chance of dying this year from 5 percent to 2 percent, then the chance of dying in a future year would increase from 95 percent to 98 percent. In general, a regulation may reduce individuals' hazard function (the chance of dying at specific dates or ages conditional on being alive). This shift in the hazard can be expressed as a reduction in the expected number of deaths in a specified time period (less than one for an individual) or as an increase in the expected number of years lived; the individual's WTP for the shift in the hazard can be expressed as a VSL or a VSLY by dividing WTP by the expected change in deaths or years lived (see Hammitt 2007).

FIGURE 3.2. SELECTION CRITERIA FOR VSL STUDIES

General Criteria
1. Be publicly available.
2. Be written in English.
3. Provide estimates for the general U.S. population.

Criteria for Revealed Preference Studies
4. Use hedonic methods that address the trade-off between wages and job-related risks.
5. Control for potentially confounding factors, such as nonfatal injury risk as well as both industry and occupation.
6. Rely on high quality risk data, equal or superior to the Census of Fatal Occupational Injuries.

Criteria for Stated Preference Studies
7. Elicit values for private risk reductions that accrue to the respondent.
8. Express the risk change as a probability.
9. Estimate willingness to pay, not willingness to accept compensation.
10. Provide evidence of validity, including sensitivity of willingness to pay to changes in risk magnitude.

The review yielded six revealed preference studies that meet the selection criteria, all of which consider the trade-off between wages and occupational risks, as well as one meta-analysis of these studies.[27] Of the stated preference studies, three met the selection criteria.[28] These latter studies consider fatal risks associated with motor vehicle accidents, ingesting pesticide residues on food, and unspecified causes. One considers only fatal injuries, the other two also address illness-related fatalities.

When adjusted for inflation and real income growth, the VSLs highlighted in these studies range from $4.4 million to $14.2 million, with a mid-point of $9.3 million (2014 dollars and income levels).[29] Applying these results in HHS analyses requires additional adjustments, as described below.

3.2.3 RECOMMENDED VALUES

The range of VSL estimates that result from this review form the basis for HHS' approach for valuing mortality risk reductions; HHS anticipates periodically updating these estimates to reflect the results from new research. This section discusses issues related to adapting these values for application in different regulatory contexts and in different years. The approach it discusses should be applied in all HHS RIAs to provide a common reference case that is comparable across analyses. However, analysts may also report results using alternative estimates or assumptions, if well-justified given the characteristics of the policy and the available research.[30]

WHAT VSL SHOULD BE APPLIED IN HHS ANALYSES?

For analyses conducted in 2014 dollars, risk reductions that occur in 2016 should be valued using a central VSL estimate of $9.6 million. Analysts should test the sensitivity of their results to values of $4.5 million and $14.6 million. The text describes how to adjust these values for other years.

We expect the VSL to vary depending on individual characteristics such as age and health status, and on risk characteristics such as whether death occurs immediately or after an extended illness. However, the effects of many of these characteristics have not been well-studied, and the results of the available research are often inconsistent. Thus the same population-average VSL should be applied in all RIAs, accompanied by discussion of

[27] The six wage-risk studies are: Viscusi (2004), Kniesner and Viscusi (2005), Hersch and Viscusi (2010), Lee and Taylor (2013), Scotton (2013), and Viscusi (2013). The meta-analysis of wage-risk studies is Viscusi (2015).

[28] The three stated preference studies are Corso, Hammitt, and Graham (2001), Hammitt and Haninger (2010), and Cameron and DeShazo (2013).

[29] The estimates reported in Robinson and Hammitt (2016) ranged from $4.2 million to $13.7 million, with a mid-point of $9.0 million (2013 dollars and income levels). They have been updated to 2014 dollars and income levels in these *Guidelines*, using the approach described below.

[30] See Chapter 6 for more discussion of the analysis of uncertainties.

uncertainties.[31] The values cited above should be adjusted for inflation and real income growth as well as for latency or cessation lag if relevant.[32] Sensitivity analysis also should be conducted in cases where the individuals affected are predominantly very young or very old. Each of these adjustments is discussed below.

The first set of adjustments is needed to reflect the time that has elapsed since the VSL studies were conducted, and involve addressing both inflation and changes in real income. The process for inflating values to reflect economy-wide price levels as of a common dollar year is discussed in Chapter 5.[33] Adjusting for real income growth is a separate step that requires two inputs: an estimate of the change in population-wide real income per person, and an estimate of the extent to which WTP is expected to change in response to the income change. The latter is generally expressed as the percentage change in the VSL associated with a one percent change in real income; i.e., the income elasticity.

Although both economic theory and numerous empirical studies suggest that the VSL increases as real income increases, the rate of increase is uncertain (Hammitt and Robinson 2011, DOT 2015a). Some research suggests that a one percent change in income leads to less than a one percent change in the VSL (e.g., Viscusi and Aldy 2003), and other research suggests that it leads to more than a one percent change (e.g., Kniesner, Viscusi and Ziliak 2010, Viscusi 2015). Given this uncertainty, HHS analysts should apply an income elasticity of 1.0 in their analyses.[34]

Once the VSL has been inflated to the common dollar year used in the analysis, the formula for adjusting for real income growth (assuming a constant rate of income growth and a constant income elasticity) is:

$$VSL(year\ y) = VSL(year\ x) * (1+real\ income\ growth\ rate)^{elasticity\ *\ (y-x)}$$

Because no single source provides data on both actual and projected changes in real income, analysts will need to use different sources depending on the time period. More specifically, analysts should use Current Population Survey (CPS) data to adjust for past income growth, and Congressional Budget Office (CBO) data to adjust for future income growth; both focus on earnings, consistent with the measures generally used in the VSL studies.[35] The most recent CBO report (2015, p. 112) projects real earnings growth at 1.4 percent per year for 2015 through 2040.

Table 3.1 provides an example of the adjustments to these values over a 10-year period using the data sources identified above, including a VSL income elasticity of 1.0 and real income growth of 1.4 percent per year. (Note that while values should be inflated only to the common dollar year used in the analysis (2014 in this example), the adjustment for real income growth is needed for each subsequent year that the analysis covers.) As indicated by the table, if the analysis is conducted in 2014 dollars, mortality risk reductions that accrue in 2016 would be valued using a central VSL estimate of $9.6 million. At minimum, analysts should test the sensitivity of their results to the values at the low and high ends of the range; i.e., $4.5 million and $14.6 million.

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[31] This implies there should be no adjustment for morbidity prior to death for fatal cases. If regulation of a hazard (such as a foodborne pathogen) can prevent both fatal and nonfatal illness, the expected reduction in fatal cases should be valued using the VSL and the expected reduction in nonfatal cases should be valued using appropriate estimates of WTP or monetized QALYs as discussed in Section 3.3.

[32] Latency is the time between when an individual is exposed to a hazard and when the adverse effect results; cessation lag is the time between when an individual's exposure to a hazard ends (or is reduced) and when his or her risk of adverse effect declines. These time periods are not necessarily equal.

[33] The calculations in the text use the Consumer Price Index (CPI, available at http://www.bls.gov/cpi/) to adjust for inflation. As discussed in Chapter 5, analysts may use the Gross Domestic Product implicit price deflator instead of the CPI.

[34] If changing the income elasticity estimate is likely to substantially change the analytic results, analysts should explore the effects of applying alternative elasticities.

[35] More specifically, for income growth in prior years, analysts should use CPS data on the annual median usual weekly earnings of employed wage and salary workers, for fulltime workers (usual working hours over 35), reported on an average per capita basis in constant dollars, which are available at http://www.bls.gov/cps/earnings.htm. For income growth in future years, analysts should use the estimates in the CBO Long-Term Budget Outlook. The 2015 CBO report is available at https://www.cbo.gov/publication/50250. See Chapter 4 of these *Guidelines* for more discussion of the use of median versus mean values.

TABLE 3.1. VSL ESTIMATES BY YEAR (2014 DOLLARS)

YEAR	LOW VSL ESTIMATE	CENTRAL VSL ESTIMATE	HIGH VSL ESTIMATE
2014	$4.4 million	$9.3 million	$14.2 million
2015	$4.4 million	$9.5 million	$14.4 million
2016	$4.5 million	$9.6 million	$14.6 million
2017	$4.5 million	$9.7 million	$14.8 million
2018	$4.6 million	$9.9 million	$15.0 million
2019	$4.7 million	$10.0 million	$15.2 million
2020	$4.7 million	$10.1 million	$15.4 million
2021	$4.8 million	$10.3 million	$15.6 million
2022	$4.9 million	$10.4 million	$15.9 million
2023	$4.9 million	$10.6 million	$16.1 million
Note: See text for discussion of assumptions and calculations.			

Thus if a regulation reduced the number of statistical cases of premature mortality by 75 in 2016, applying the central VSL estimate would result in benefits of $720.0 million (75*$9.6 million), with a low of $337.5 million (75*$4.5 million) and a high of $1,095.0 million (75*$14.6 million).

In some cases, analysts may also need to adjust the VSL estimates to reflect a lag or delay between when exposure to a hazard is reduced and when the risk change occurs. If the risk reduction is expected to occur in the same year that the regulatory costs are incurred, then the VSL for that year should be applied. If the risk change occurs later, then the VSL should be applied at the time when the risk change occurs, rather than in the year in which the associated regulatory costs are incurred.[36] In other words, using the values above, if both the costs and the risk reductions occur in 2016, than $9.6 million would be used as the central VSL estimate. If instead the costs are incurred in 2016 but the risk reduction does not occur until 2018, then the central estimate would be $9.9 million, which would be discounted back to 2016 for comparison with the costs incurred in that year, using the same discount rate as applied elsewhere in the analysis. Recommended rates, as well as the mechanics of discounting, are discussed in Chapter 5.

Finally, some regulations may predominantly affect the very young or very old, rather than those of all ages. In these cases, the age distribution of those affected is likely to differ significantly from the age of those included in the VSL studies that underlie the approach discussed above, which often address individuals between the ages of 18 and 65 (with some exceptions). There is substantial uncertainty regarding how VSL varies with age (see, for example, Aldy and Viscusi 2007, Krupnick 2007, and Hammitt 2007; Robinson and Hammitt 2016 discuss related theory and empirical research in more detail).

If a regulation largely affects the very young or the very old, analysts should at minimum provide a supplemental sensitivity analysis based on estimates of the expected value of future quality-adjusted life years (QALYs).[37] In other words, regulations that primarily affect young children or the elderly should include two calculations: a primary benefit estimate based on the VSL recommendations in this section, and a sensitivity analysis based on monetized QALY estimates, which are discussed in detail in the next section. In this sensitivity analysis, the value per QALY is multiplied by the present value of the expected life year gain.[38]

In addition to the uncertainties represented by the ranges of values and adjustments discussed above, analysts should provide a qualitative discussion of the other limitations of this approach. The major limitations include differences in the types of risks addressed in the underlying studies and those addressed by the particular policy,

[36] As noted earlier, this delay is described as the "cessation lag" when it refers to risk reductions rather than risk increases.

[37] Analysts may also explore the effects of alternative assumptions regarding the relationship between the VSL and age or life expectancy, if clearly explained and well-justified. Many analyses have used a VSLY estimate rather than an estimated value per QALY to explore these effects.

[38] Such sensitivity analysis would not noticeably change the results if the age distribution of those affected by the regulation is similar to the U.S. age distribution, as long as the value per QALY (or VSLY) is calculated from a population-average VSL.

as well as in the population affected. Thus this approach may over- or understate the value of mortality risk reductions. Where the analytic conclusions are particularly sensitive to the approach used to value mortality risks, analysts may also wish to conduct breakeven analysis to identify the VSL at which the costs would be equal to the benefits, as discussed in Chapter 6.

3.3 VALUING MORBIDITY RISK REDUCTIONS

Valuing morbidity risk reductions is more complicated than valuing mortality risk reductions for two reasons. First, morbidity risks are more diverse, differing in duration and severity as well as in the attributes of health that are affected (e.g., physical or cognitive functioning). Second, high quality WTP estimates are not available for many morbidity risks, requiring the use of proxy measures. Thus, as discussed below, HHS analysts should first review the literature to determine whether WTP estimates of reasonable quality are available for risks similar to those addressed by the regulation, applying the benefit transfer framework described previously.[39]

HOW SHOULD MORBIDITY RISK REDUCTIONS BE VALUED?

Analysts should first review the literature to determine whether suitable WTP estimates of reasonable quality are available. If not, they should use monetized QALYs as a proxy, following the approach described in this section.

If such estimates are not available, analysts should instead apply values that combine estimates of the resulting QALY gain with estimates of the monetary value per QALY. Cost-savings that are not reflected in the QALY measure may be added to these values, including those that accrue to third parties (such as savings in insured medical costs). Because of the diversity of the health effects and the gaps in the research literature, the discussion that follows focuses on the approach analysts should follow to develop estimates, rather than recommending values for particular health conditions.

3.3.1 QUALITY-ADJUSTED LIFE YEARS

The QALY is a nonmonetary measure that integrates the duration and severity of illness. QALYs are widely used to rank and prioritize public health programs, analyze the cost-effectiveness of health policy and medical treatment decisions, and compare health status across individuals or population groups. In these contexts, QALYs are generally not assigned a monetary value, but monetization is needed to apply these estimates in regulatory analysis.[40]

QALYs are derived by multiplying the amount of time an individual spends in a health state by a measure of the health-related quality of life (HRQL) associated with that state. HRQL is estimated using a scale anchored at zero and one, where one corresponds to full health and zero corresponds to a state that is as bad as dead (values cannot be greater than one but may be less than zero for states that are judged to be worse than dead). In principle, the HRQL associated with a health state may vary among individuals, but in practice a common value is used for each health state. Expected QALYs are then calculated by weighting the HRQL experienced in each future year of life by the probability of living in that year (i.e., by the survival curve).[41] In addition, future QALYs are usually discounted using the same rates as applied to monetary values. Appendix C provides more information on the estimation of QALYs.

Once HRQL is determined for a particular health state and multiplied by the duration of that state, the resulting QALYs can be summed across the health states (e.g., acute and chronic phases) associated with a particular illness, and across the illnesses associated with a particular hazard. For example, for foodborne illness, QALYs

[39] Due to the lack of a reasonably recent and comprehensive review of this research, analysts will need to search bibliographic databases, such as EconLit (http://www.aeaweb.org/econlit/index.php) and EVRI (https://www.evri.ca/Global/HomeAnonymous.aspx), to identify potentially applicable studies and conduct a criteria-driven review that follows the benefit transfer framework introduced above.

[40] In cost-effectiveness analysis, valuation is implicit, because monetary thresholds are needed for comparison to the cost-effectiveness ratio to determine whether an intervention is worth implementing. In addition, valuation is implicit in any policy decision that results, which involves choosing to fund a particular invention rather than using the money for other goods or services.

[41] For the U.S. population, survival curves are updated annually by the CDC; see http://www.cdc.gov/nchs/products/life_tables.htm.

can be summed across cases of acute gastrointestinal illness, including those that do and do not require hospitalization, as well as more severe effects. For regulatory analysis, health status with the regulation or other policy must be compared to health status in the absence of the regulation, which is likely to be less than full health. In particular, health status generally deteriorates with age, so that average HRQL for older individuals is generally less than 1.0 (see Hamner et al. 2006). Some regulations may also target individuals with pre-existing conditions or lifestyle characteristics that will not be ameliorated by the regulation.

An example of these calculations is provided in Figure 3.3. For simplicity, in this example we do not discount future impacts; however, as discussed in Chapter 5, discounting should be used to reflect time preferences when similar calculations are performed in regulatory analyses.

FIGURE 3.3. EXAMPLE OF QALY CALCULATIONS

- Assume that, in the absence of the policy, the average individual affected will experience health-related quality of life of 0.7 throughout their estimated remaining life span of 20 years.
- With the policy, assume that the average individual affected will instead experience health-related quality of life of 0.9 over the same time period
- The QALY gain attributable to the policy is the difference between 20 years with a health status of 0.9 (18 QALYs) and 20 years with a health status of 0.7 (14 QALYs), which equals 4.0 QALYs, prior to discounting.

The research base for estimating QALYs is extensive, including numerous primary research studies as well as population databases that collect HRQL data for a wide range of conditions. Thus regulatory analysts can generally rely on existing research to estimate the QALY gains associated with reducing the risks of various types of morbidity.[42] Estimates from many previously completed studies can be found in the Tufts Cost Effectiveness Analysis (CEA) Registry (described in Thorat et al. 2012), using the benefit transfer process discussed earlier to assess their quality and applicability. However, this database does not include studies that estimate QALYs or HRQL without comparison to costs, so analysts should search the research literature to identify other potentially applicable studies.

Another option is to rely on population-wide surveys. Some large national surveys (such as the U.S. Medical Expenditure Panel Survey or MEPS) have at times included one or more of the generic HRQL indices, such as the EQ-5D which is described in more detail in Appendix C. These HRQL estimates can then be multiplied by duration estimates from research on the health state of concern. Relying on such surveys can be particularly useful for regulatory analysis, because they provide consistently-derived estimates across a wide range of outcomes and enable analysts to control statistically for the effects of other factors (such as age and co-morbidities) on HRQL.[43] For some health effects, however, these surveys may not include enough cases to reliably estimate HRQL.

A 2006 Institute of Medicine report provides more detailed discussion of these measures and their application in regulatory analysis, recommending factors that should be considered in selecting among the available sources of HRQL and QALY estimates. In particular, to the extent possible, QALY estimates should satisfy the criteria listed in Figure 3.4.

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[42] In those rare cases where suitable estimates are unavailable, analysts may need to rely on expert judgment to estimate the QALY gains associated with the regulation. Analysts should apply the EQ-5D index with U.S. weights when implementing this approach.

[43] For example, EQ-5D scores for a large number of health conditions based on MEPS are provided in Sullivan and Ghushchyan (2006). This article, and a calculator that allows users to retrieve EQ-5D scores by International Classification of Disease code and demographic characteristics, is available online at http://www.ohsu.edu/epc/mdm/webResources.cfm.

FIGURE 3.4. SELECTION CRITERIA FOR QALY ESTIMATES

1) QALY estimates should be based on research that addresses the risks and populations affected by the regulation.
2) The description of the effects of the health state on quality of life should be based on information from those who have experienced the condition (such as patients).
3) The preference weights placed on the health states should be based on a survey representative of the general U.S. population.
4) The "without new regulation" baseline (with the condition) should be compared to a realistic estimate of "with-regulation" health status, which takes into account factors (such as age and co-morbidities unrelated to the regulated hazard) that may lead those affected to be in less than perfect health once the regulation is implemented.[44]
5) The implications of related uncertainties should be discussed and addressed quantitatively if significant.

Developing approaches for measuring QALYs and testing their implementation is an active area of research. There continue to be diverse opinions on many technical issues such as the dimensions of health that should be considered, the types of survey questions that should be used to explore these dimensions, the elicitation of preferences, and the statistical analysis of the results (Lipscomb et al. 2009). Thus the approaches described above continue to evolve, and new options are under development.

3.3.2 THE VALUE OF A QALY

To use QALY estimates to value morbidity risk reductions in regulatory analysis, they must be assigned a monetary value. One approach would be to rely on emerging research that explicitly considers individual WTP per QALY (e.g., Haninger and Hammitt 2011); HHS is currently exploring this research to determine whether it is possible to develop a function that reflects how the value varies depending on factors such as the severity and duration of the effect.

In the absence of such a function, analysts often assume that the value per QALY is a constant, frequently applying a VSLY estimate, calculated by dividing the VSL by the discounted expected number of life years remaining. A preferable approach is to calculate a constant value based on expected QALYs rather than expected life years. Future QALYs are generally less than future life years because health tends to deteriorate with age. Dividing the VSL by future QALYs yields an average value per QALY larger than the VSLY (see Hirth et al. 2000).

For analyses conducted in 2014 dollars, HHS analysts should estimate the value of a QALY based on the VSLs reported in Table 3.1. For analyses that use a different dollar year, the VSL estimates will first need to be adjusted to reflect inflation and real income growth, as discussed earlier.

Based on data reported in the underlying VSL studies, analysts should assume that the average individual in these studies is 40 years of age. Table 3.2 reports the value of a QALY that results when health-related quality of life in each subsequent year is estimated using the U.S. EQ-5D results reported in Hamner et al. (2006) and the conditional likelihood of survival for each year of age is based on the population-averages in Arias (2014).[45] The value of future years should be discounted at the same rates as used elsewhere in the analysis. The table provides the results of these calculations for risk reductions that occur in 2016, in 2014 dollars.[46]

[44] This point is of particular importance in regulatory analysis, which is intended to realistically reflect the health of the affected population without and with the policy. In the absence of regulation, this population may suffer from a variety of health conditions, some of which will not be affected by the policy change. For example, a food safety regulation that targets the risk of gastrointestinal illness is not likely to affect air pollution-related respiratory effects. In addition, health status generally declines with age. Thus the average health of the affected population is likely to be less than perfect health (i.e., less than HRQL = 1.0) even after the regulation becomes effective.

[45] Arias (2014) provides life tables for 2009. Updated values may be used when available; see: http://www.cdc.gov/nchs/products/life_tables.htm.

[46] Many previous analyses value QALYs using a constant VSLY rather than the value per QALY presented here. As noted earlier, both are calculated from a VSL based on the average life expectancy of the individuals studied. The difference is that the resulting VSLY estimate implicitly averages over future health, while the value per QALY estimate takes into account the expected decline in health status associated with aging.

TABLE 3.2. VALUE PER QALY IN 2016 (2014 DOLLARS)

VSL	VALUE PER QALY	
	3% DISCOUNT RATE	7% DISCOUNT RATE
$4.5 million	$230,000	$380,000
$9.6 million	$490,000	$820,000
$14.6 million	$750,000	$1,200,000

For example, if a regulation leads to a 0.2 QALY gain per affected individual on average in 2016, then applying the central VSL estimate (using a 3 percent discount rate) from Table 3.2, the value of that gain would be $98,000 (0.2*$490,000). If the gain accrues to 75 members of the population, than the total value of the risk reduction would be $7,350,000 (75*$98,000).

Estimates of the averted costs of illness may be added to estimates of WTP or monetized QALYs, as long as the same cost-savings are not counted elsewhere in the analysis (see Chapter 4 for more discussion of medical costs).[47] These cost estimates should always be reported as a separate line item in the RIA, so that their treatment is clear. If a WTP study is used for valuation, the analysts should review the study to ensure that the costs are not already captured in the WTP estimates. Typically, WTP studies may capture out-of-pocket costs and lost earnings, and possibly informal care provided by household members, but do not include costs paid by third parties, such as medical expenses paid by insurance. If a regulation reduces these costs, the savings can be added to the WTP estimate. Any cost-savings included in the analysis of regulatory costs should not also be added to the benefit estimates.

If monetized QALYs are used for valuation, the extent to which costs are included is highly uncertain given that the measure does not directly reflect monetary consequences. Occasionally, studies that estimate HRQL instruct respondents to assume their medical costs and lost income will be offset by insurance. In the absence of more specific information, analysts may add medical costs paid by third parties to the monetized QALYs, but should not add estimates of lost productivity or income to avoid potential double-counting.

Estimates based on QALYs monetized using a constant value are likely to be less accurate than approaches based on direct estimation of WTP, but may provide a reasonable proxy when WTP estimates are unavailable. The limitations of this approach relate in part to the characteristics of the QALY measure and in part to the approach used for valuation, and should be discussed when documenting the analysis.

The construction of the QALY assumes that how individuals value health states is independent of the duration of the state, the age at which it is experienced, the individual's remaining life expectancy, and his or her wealth and income (Hammitt 2002, 2013, Institute of Medicine 2006). Moreover, QALYs do not explicitly account for the changes in wealth or income that result from changes in health, nor for how individuals are willing to trade off spending on particular risk reductions versus spending on other goods and services.

[47] For some rules, whether medical costs should be counted as a "cost" or "benefit" will be uncertain, and analysts will need to be clear about how these costs are treated when documenting the analysis. Generally, if changes in medical costs are part of the implementation of the requirements (i.e., a policy input), then they should be counted on the cost-side of the equation. If they are one of the policy outcomes, then they should be included in the benefit calculation.

In addition, relying on a constant value per QALY does not reflect the likely variation in value due to factors such as duration and severity.[48] More research is needed to develop a valuation function for QALYs that better approximates individual WTP for risk reductions.

Given the above discussion, HHS analysts should first consult the WTP research to determine whether suitable estimates are available for the morbidity risk reductions of concern. If not, they may use monetized QALYs as a proxy, recognizing that we are uncertain whether the resulting values under- or overstate individual WTP for the risk reduction. Regardless of whether WTP or monetized QALY estimates are applied, analysts should document any concerns about the quality or applicability of the selected studies.

[48] Given these concerns, an expert panel recommended against assigning monetary values to QALYs in regulatory analysis (Institute of Medicine, 2006); however, OMB has not amended *Circular A-4* to adopt this recommendation. It continues to suggest that the use of monetized QALYs is acceptable as long as analysts acknowledge the limitations of the approach.

Chapter 4

Assess Costs

HHS regulations may impose costs on individuals, industries, other organizations (both for-profit and nonprofit), and government entities. In some cases, costs may be offset by savings; for example if a regulation reduces or streamlines existing requirements by replacing paper with electronic recordkeeping and reporting.[49] This chapter begins by describing some basic concepts that are particularly important when estimating costs. It then describes approaches for estimating the most common types of costs in more detail.

4.1 BASIC CONCEPTS AND APPROACH

Below, we describe economic concepts that are of particular importance when estimating costs: opportunity costs, transfers, and producer surplus. A discussion of the general approach to the cost analysis follows.

4.1.1 ECONOMIC FOUNDATION

Three fundamental notions from economic theory are of particular importance in assessing costs. The first is that economists measure costs by the value of forgone opportunities. In other words, costs are incurred when resources are used for one purpose and hence cannot be used for another purpose. The opportunity costs are the value of the benefits that could have been provided by devoting the resources to their best alternative use. This interpretation differs from the concept of accounting costs (i.e., actual expenses plus depreciation of capital equipment). It is consistent with the concept of WTP, as discussed in Chapter 3.

The second is the distinction between resource costs and transfers. Transfers are monetary payments between persons or groups that do not affect the total resources available to society.[50] They are a benefit to recipients and a cost to payers, with zero net effect. For example, some types of taxes, fees, and surcharges can be categorized as transfer payments. Such transfers often can be ignored in benefit-cost analysis, as long as they do not lead to behavioral changes that significantly affect the calculation of net benefits. However, transfers should be included in the distributional analysis, as discussed in Chapter 7.

OPPORTUNITY COST VERSUS ACCOUNTING COST

Opportunity costs are easy to confuse with accounting costs. Some may argue that a proposed regulation will not have any "costs" because regulated entities will simply re-allocate existing resources to comply with the regulation; no new expenditures are incurred.

However, if resources are shifted for compliance purposes, other productive uses of those resources are forgone. If labor is shifted to compliance from production, for example, the opportunity cost is the value of forgone production.

Where the imposition of transfer payments affects behavior, associated impacts should be taken into account in the benefit-cost analysis. For example, reductions in government payments to hospitals would often be viewed as a transfer. However, the affected hospitals may accept fewer patients or use less expensive treatments, in turn affecting health outcomes. This change in health should be addressed in the benefit-cost analysis, if significant. Similarly, taxes can also change behavior; for example, taxes on wages provide a disincentive for working and higher taxes may lead more people to stay out of the labor force.[51] In addition, transfers involve transaction costs that may be significant in some cases. When identifying the costs to be

[49] As discussed in Chapter 2, analysts should decide whether to report offsetting cost savings as negative costs or positive benefits depending on whether these savings relate to the inputs needed to achieve regulatory goals, or the outcomes associated with those goals.

[50] Because RIAs focus on the effects on the U.S. population, transfers from the United States to other nations, and from other nations to the United States, should be included in the benefit-cost analysis.

[51] HHS regulations rarely, if ever, affect tax rates. If such rates are affected, analysts may wish to consult Boardman et al. (2011) and other resources on estimating the associated deadweight loss, typically referenced as the marginal excess tax burden.

quantified, analysts should consider the potential for significant net losses or gains nationally resulting from the imposition of transfer payments.[52]

The third fundamental notion is the difference between compliance costs and changes in producer and consumer surplus. As introduced in Chapter 3 and discussed in Appendix B, consumer surplus is the benefit that consumers receive when they are able to purchase products for less than they are willing to pay; producer surplus is the difference between the revenue producers receive and their cost of production. When a regulation increases production costs, the market price is likely to increase, inducing consumers to reduce their consumption and producers to reduce production. The cost of the regulation includes both the direct compliance costs and the "deadweight loss" associated with the reduction in output. However, regulation often has negligible impact on prices, in which case the deadweight loss will be quite small and compliance costs will be a reasonable approximation of total costs. We return to this issue later in this chapter, when discussing the use of partial and general equilibrium models.

4.1.2 GENERAL APPROACH

Social cost is the sum of the resource costs incurred as a result of implementing the regulation. These costs may include costs incurred by regulated entities in the form of resources (labor, material, equipment) used to comply with the regulation, valued by their opportunity costs. Social cost may also include costs incurred by governments to implement and enforce the regulation. Other effects, such as consumer decisions to replace the regulated product with a substitute, may also occur in response to the compliance costs.

In principle, analysts could develop a model that includes all the interactions between regulated entities, consumers, and related markets to capture the total social cost of a regulation. However, such analysis is usually impractical given data, time, and resource constraints. Furthermore, most regulations are likely to have negligible impacts on price, in which case such complex modeling is not necessary to understand key impacts. During the framing and screening process (see Chapter 2), analysts should determine the cost categories of interest and the modeling techniques to be applied, recognizing that this is an iterative process. Changes in the approach may be needed as more is learned about the potential impact of the policy options. Nonquantified costs, as well as the reason for not quantifying them, should be reported as well (see Chapter 6).

In most cases, the analysis focuses on estimating the incremental compliance costs incurred by the regulated entities, assuming full compliance with the regulation, and government costs.[53] Compliance costs include the resources used by the regulated entities to comply with the regulation. These costs often account for the largest proportion of social costs and are an important input into the supplemental analyses discussed in Chapter 7. The analysis should also include costs incurred by the government. Such costs generally involve guiding and monitoring implementation of the regulation, as well as providing information and training as needed. In some cases, the government may have an ongoing operational role; for example, it may provide services in addition to those provided by the regulated community. Government costs also include enforcing the regulation through activities such as inspections and reporting requirements. When significant, these government costs should be quantified.

If compliance costs are significant on a per entity or industry basis, they may result in other impacts. If these additional effects are sufficiently large, they should be quantified. For example:

- Compliance costs may result in substituting behaviors. If industry or consumers shift to alternative products, or if industry develops new products to replace the regulated products, analysts should consider the net effect on society.

[52] As noted in Chapter 1, an RIA is required for regulations resulting in significant transfers, because of the additional costs or benefits that may result.

[53] Analysts should consider the uncertainty associated with an assumption of full compliance and provide analysis of alternative assumptions, as appropriate.

- Compliance costs may result in changes in available services, which could result in additional, and possibly non-pecuniary, costs (e.g., time losses associated with needing to find new doctors or traveling farther for treatment). Such costs should also be taken into account.[54]

Finally, care should be taken to identify transfer payments as discussed earlier. For example, proposed regulations may require the payment of fees to HHS agencies for processing paperwork or adjudicating claims. The fees may be set to recover the HHS labor and other costs associated with administering the program. If the opportunity cost to HHS of administering the requirement is already captured in the analysis, the fees represent a transfer payment that should not be counted. However, if the HHS opportunity costs are not separately calculated, then the fees paid by regulated entities might be a reasonable proxy for these opportunity costs and should be included as a social cost.

4.2 ASSESSING COMPLIANCE AND GOVERNMENT IMPLEMENTATION COSTS

Chapter 2 discusses the screening process used to identify key cost categories. Typical categories include administrative costs (including time, materials, and travel), capital and operations costs, and medical costs. As discussed above, government implementation costs should also be considered.

4.2.1 ADMINISTRATIVE COSTS

Most regulations impose administrative costs on regulated entities or the implementing government agency. Related activities may include, for example, reviewing the new regulations, developing protocols for compliance, collecting and reporting data, and training staff on implementation. The following sections describe how to quantify and monetize the components of these costs, including estimating the amount of time required for administrative tasks, valuing this time in monetary terms, and locating data on administrative expenditures.

Amount of time required: Estimating the amount of time needed to comply with administrative requirements is relatively straightforward.[55] Usually, time should be measured in terms of "hours" so that the quantity can be easily combined with information on the value of time, which is generally measured in terms of hourly compensation (see below).[56] Analysts may obtain estimates of the number of hours needed to review the requirements, fill out forms, transmit data, or complete other similar tasks using surveys, information interviews, past analysis, or Information Collection Requests (see Chapter 7). Who is undertaking these activities is also important, as it affects the monetary value of time. Finally, care must be taken to ensure that the hours estimates reflect the net effect of the regulation. For example, the regulation may require that workers discontinue some activities (e.g., completing paper forms) and replace them with others (e.g., maintaining records electronically). The time saved by discontinuing activities will offset time spent on the new activities to some extent.

Table 4.1 lists the types of administrative tasks that may result from new regulations and provides suggestions for quantifying the amount of time associated with each task, noting associated costs (such as travel or materials) that should also be addressed. Time spent complying with a regulation may vary by establishment type or size. Thus, analysts should explore differences across key groups. In addition to providing more accurate cost estimates, this information is used in the supporting analyses that address impacts on entities of differing sizes and types (see Chapter 7).

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[54] For a detailed discussion of the identification and assessment of secondary effects, see Chapter 5 of Boardman et al. (2011).

[55] The same general approach can be used when regulations affect other types of time use.

[56] For rules requiring substantial amounts of labor, such as the hiring of additional, full-time employees, analysts might instead estimate the number of new employees needed and annual salaries using the data sources identified in the next section.

TABLE 4.1. TYPICAL ADMINISTRATIVE TASKS

ADMINISTRATIVE TASK	EXAMPLES OF SOURCES OR METHODS USED FOR QUANTIFICATION
Regulation and Guidance Review: All regulated entities, including those who incur no other compliance costs, will require time to read and interpret the regulation.	• Interview representatives of the affected community to obtain estimates of the amount of time required to review regulations, including time spent by legal or technical experts. • Review prior agency analyses for relevant data or conduct other literature reviews. • Assume reviewers read at the average adult reading speed (approximately 200 to 250 words per minute) and allow time for both review and interpretation.
Development or Revision of Standard Operating Procedures (SOPs): The affected entities may need to devise a compliance plan that may require them to change their SOPs. SOPs are "detailed, written instructions to achieve uniformity of the performance of a specific function" (International Conference on Harmonization).	• Interview the affected community to obtain estimates of the amount of time required to review and revise SOPs. • Review prior agency analyses for relevant data or conduct other literature reviews.
Training: Once new SOPs are established, entities will spend time training staff on how to implement the regulation.	• Interview the affected community to obtain estimates of the amount of time required for training. • Review prior agency analyses for relevant data or conduct other literature reviews. • Note that training may also require travel costs.
Sampling and Testing: A regulation may require entities to sample or test materials.	• Contact third party vendors to obtain estimates of sampling or testing costs. In such cases, the cost per test likely includes both labor and materials. • Some entities may be able to conduct the testing more cheaply using in-house staff. Interviews with the affected community may provide data on the amount of time required. In these cases, material costs should be added.
Record Keeping and Reporting: Some rules require entities to perform additional record keeping to track training, inspections, and infractions. In addition, entities may be required to submit recurring reports to the regulating agency.	• Interview the affected community to obtain estimates of the amount of time required for record keeping and reporting. • Review prior agency analyses for relevant data or conduct other literature reviews. • Note that record keeping may also result in substantial storage costs.

Valuing time: Once the amount of time needed has been calculated, analysts multiply these hours by a per hour value of time. This value will vary depending on the characteristics of the activities, the preferences of those affected, the duration of the activities, and other factors. As in other components of the analysis, the approach to valuation requires comparing the value of time use with and without the regulation, to calculate the opportunity costs the regulation imposes.

In RIAs, as in other types of analysis, time use is often valued based on simplifying assumptions that allow analysts to use readily accessible data on compensation. We introduce the default assumptions for HHS analyses below, then discuss their implications in more detail. If the characteristics of the regulation and the available data justify a different approach, the rationale for the approach should be included in the RIA along with the detailed calculations.

The value of time is an active area of research, and HHS is now working on a project that will further explore these values. [57] This new work will investigate the extent to which the default values discussed in this section appropriately measure different types of time use, including the suitable treatment of overhead costs. In the interim, analysts should apply the default values described below. Regardless of the approach used, the assumptions and related uncertainties should be addressed as discussed in Chapter 6.

[57] See Boardman (2011) and DOT (2015b) for more discussion of the related literature.

The starting point for valuing changes in time use involves distinguishing between paid and unpaid time; i.e., between market production and nonmarket activities including leisure, household tasks, and volunteer work. The first default assumption is that regulatory activities undertaken by paid employees will displace other paid work tasks, while activities undertaken during non-work time will replace other unpaid activities. In other words, the work-related administrative requirements likely to be imposed by HHS regulations (e.g., completing additional reports) would not require that the affected individuals spend more time at work and less time on leisure activities; instead they would spend less time on other tasks associated with their current occupation and the employer might rearrange work assignments. If new employees are hired, this approach assumes that the activities required for regulatory compliance would replace the activities they pursued in their previous job; those hired would be transitioning between similar jobs rather than moving from unemployment to employment.

The second default assumption is that average or median estimates appropriately measure the value of a marginal unit of time. In reality, this marginal value will likely vary based on a variety of factors, such as the amount of time (e.g., a few hours versus days or months) or the types of time use affected. However, marginal estimates generally are not readily available; most easily accessible data sources provide averages or medians.

The third default assumption is that the value of activities conducted during paid work time can be best approximated by the cost of labor to the employer. The standard economic model assumes that employers are willing to incur labor costs equal to the value of workers' marginal product. Conceptually, this amount represents the value of what the employee would have otherwise produced in the absence of the regulation. Thus the opportunity cost of paid work time can be approximated based on the employer costs, including pay, benefits, taxes, and associated overhead.

The fourth default assumption is that the opportunity cost of unpaid time can be best approximated by post-tax wages. Consistent with the standard economic model, this approach assumes that individuals decide whether to engage in paid work depending on whether the incremental income exceeds the value they place on unpaid time, a decision generally described as the labor-leisure trade-off. Taxes and benefits are usually excluded from this calculation, assuming that individuals focus on their take-home pay in making related decisions. In other words, an additional hour of paid work is valued differently by the employee than the employer, because many costs to the employer are not received by employees (e.g., income and payroll taxes) or may not be visible to the employees (e.g., benefits) and hence are unlikely to be taken into account in their decision-making. As is the case throughout the analysis, particularly if the value placed on time use significantly influences the analytic conclusions, then the approaches discussed in Chapter 6 should be used to assess the implications of related uncertainties.[58]

Table 4.2 summarizes the assumptions used to develop default estimates of the value per hour of time. Below, we discuss these assumptions in greater detail.

[58] Estimating the value of time for individuals who are not active in the labor market, such as children or seniors, is particularly challenging. As discussed later in this chapter, analysts should apply the same approach for valuing non-work time to all individuals.

TABLE 4.2. CONSTRUCTING DEFAULT ESTIMATES OF THE VALUE OF TIME

CONTEXT	COSTS INCLUDED IN HOURLY VALUE	DATA SOURCES AND KEY ASSUMPTIONS
Employees undertaking administrative tasks while working	• Pre-tax wages	• OES or NCS ECEC data on wages
	• Benefits: - Paid time off - Health benefits - Retirement benefits - Other legally required benefits - Payroll taxes • Other overhead costs: - General and administrative (G&A) - Fixed overhead - Insurance - Accounting profit	• Industry-specific data as available, or assume benefits plus other overhead costs equal 100 percent of pre-tax wages (i.e., for a fully-loaded wage rate, multiply pre-tax wages by a factor of "2")
Individuals undertaking administrative tasks on their own time	• Post-tax wages	• OES or NCS ECEC data on wages • Adjust wage estimates using data on household income before and after taxes collected in the CPS
Acronyms: CPS – Current Population Survey, available at http://www.census.gov/cps/data/cpstablecreator.html (U.S. Census Bureau) ECEC – Employer Costs for Employee Compensation, available at http://www.bls.gov/ncs/ect/ (U.S. Bureau of Labor Statistics) NCS – National Compensation Survey, available at http://www.bls.gov/ncs/ (U.S. Bureau of Labor Statistics) OES – Occupational Employment Statistics, available at http://www.bls.gov/oes/home.htm (U.S. Bureau of Labor Statistics)		

On-the-job activities: For paid work-related activities, the opportunity cost, or value, of a unit of time devoted to regulatory compliance equals the marginal value of the product that would have otherwise been produced in the absence of the regulation. Another way to frame this concept is to ask, what benefit to the economy would the employee have produced with an additional hour of time?[59] Data on this value are not readily available; however, market data on employee compensation provide a reasonable proxy.

From an employer's perspective, when making a decision about whether to hire more help, the company will think about the entire cost of the new employee, including wages, fringe benefits, and other overhead costs needed to support the employee in accomplishing the work. Thus, to estimate the value of an hour of time, analysts should sum the costs of these items. Wages (pre-tax) generally include base pay, cost-of-living allowances, guaranteed pay, hazardous-duty pay, incentive pay (commissions, bonuses), and tips.[60] Fringe benefits generally include paid time off, health benefits, retirement benefits, other legally required benefits (e.g., worker's compensation) and payroll taxes.[61] The combination of wages and fringe benefits is often referred to as the employer costs of compensation.

In addition, employers incur other costs that support labor and are not directly relatable to the production of goods and services. These costs are generally referred to as "overhead costs," and may include the following categories:

[59] Analysts should generally assume that time losses associated with HHS regulations only affect the quantity of hours worked, not the price of goods and services produced with that time. Thus, the analysis focuses on the marginal value of production associated with an hour of time. If a proposed regulation will result in time reallocations that are sufficiently large to affect the price of goods and services produced, more complex analysis may be required.

[60] Throughout the remainder of this chapter, the term "wages" is used generally to refer collectively to all of these categories.

[61] Conceptually, payroll taxes are included in this calculation because analysts need a full accounting of the total cost paid by employers for their employees' time. As explained above, this cost is used as a proxy for the value of the employees' production.

- General and administrative (G&A) costs, such as human resources, payroll, accounting, sales personnel, executive salaries, legal fees, office supplies, equipment, communications, administrative buildings, office space, travel, subscriptions, and other items related to administrative activities that support operating (production) labor;
- Fixed costs, such as building services (safety, general engineering, general plant maintenance, janitorial, cafeteria);
- Insurance costs, such as liability, property, and travel; and
- Accounting profit, which reflects the opportunity cost of equity capital.[62]

Thus combining data on wages, benefits, and other overhead costs approximates the value of time from the employer's perspective.[63]

Two data sources published by the U.S. Bureau of Labor Statistics (BLS) provide national information on hourly wages by industry sector (see bottom of Table 4.2 for hyperlinks to data sources).[64] The Occupational Employment Statistics (OES) are generated from a semiannual mail survey that covers a broad number of establishments across the United States.[65] The National Compensation Survey (NCS) is an in-person survey of a subset of establishments and provides information on quarterly changes in employer costs (the Employer Cost Index, or ECI) and cost levels (Employer Costs for Employee Compensation, or ECEC).[66,67]

Both surveys use statistical methods to collect nationally representative samples. The OES survey is larger, covering a greater range of occupations and geographic areas, and provides estimates of median, as well as mean, wages.[68] In contrast, the NCS program samples fewer establishments, but conducts the survey in-person and collects more detailed information on occupations within an establishment. In addition to reporting wage and salary information (pre-tax, average only), the NCS provides data on other compensation, including benefits (paid leave, insurance, retirement). Generally, OES is the preferred source for national estimates of hourly wages given its broader geographic coverage. The ECEC is useful for identifying compensation rates for specific categories of employees (e.g., managers).

USING MEDIAN VS MEAN WAGE DATA

Whether the median or mean (i.e., average) is the best central tendency estimate of compensation depends on the extent to which the distribution is highly skewed for workers in the occupations of concern. When considering the overall population, the average is significantly greater than the median because of the small number of people who are very highly compensated. Thus, if only a fraction of the U.S population is affected by a regulation, the best estimate may be the median (which is the center of the income distribution), rather than the mean (which is closer to the upper tail of the distribution). However, if the entire population is affected, applying the mean may be appropriate. Analysts should consider the specific characteristics of the rule when selecting the most appropriate measure.

[62] "Accounting profit" is a different concept from "economic profit." Firms require the investment of capital to operate and must provide a reasonable return on that investment, or the capital would be put to other uses. Accounting profit is a measure of the return on this capital investment. Economic profit, in contrast, equals sales revenue minus all costs, including the cost of equity capital. Under perfect competition, long-run economic profits are zero. See U.S. Environmental Protection Agency's Science Advisory Board (2007) for more discussion.

[63] Publicly-available estimates of overhead costs may include fringe benefits; thus whether to separately include benefits will depend on the data sources used in the analysis. The overhead rate discussed in this section is intended to be inclusive of fringe benefits; therefore it is applied to an estimate of wages that does not include benefits.

[64] We focus on data sources providing hourly wage data, as opposed to weekly, annual, or household estimates, to avoid the need for additional assumptions about the number of hours worked and/or the number of employed workers in a household. If data on annual salaries is required, additional sources, such as the U.S. Bureau of Labor Statistics' Quarterly Census of Employment and Wages (QCEW, available at http://www.bls.gov/cew/), may also be used.

[65] OES excludes farm establishments and self-employed persons.

[66] See http://www.bls.gov/oes/ pages on "OES Frequently Asked Questions" for a comparison of the OES and NRC.

[67] NCS excludes federal government employees.

[68] Ideally, analysts would use estimates of the marginal wage rate (i.e., the increment paid for the last hour worked) rather than the average cost across all hours worked. However, average or median values are generally used due to the lack of data on marginal rates.

Obtaining data on other overhead costs is challenging. Overhead costs vary greatly across industries and firm sizes. In addition, the precise cost elements assigned as "indirect" or "overhead" costs, as opposed to direct costs or employee wages, are subject to some interpretation at the firm level.

No readily available, national data exist on overhead rates by industry or sector. Data available in the ECEC suggest that benefits average 46 percent of wages and salaries.[69] Because this figure excludes overhead costs other than benefits, it represents a likely lower bound on the overhead rate. In the private sector, analysts often use a "rule of thumb" assumption that total overhead costs (benefits plus other overhead) equal 150 percent of wages. As a an interim default, while HHS conducts more research, analysts should assume overhead costs (including benefits) are equal to 100 percent of pre-tax wages (roughly the midpoint between 46 and 150 percent), and they should test the sensitivity of their results to alternative assumptions. Figure 4.1 provides an example of this calculation.

FIGURE 4.1. SAMPLE CALCULATION OF THE VALUE OF TIME SPENT ON A PAID ADMINISTRATIVE TASK

Assume a proposed rule will result in five additional hours each year of administrative work for occupational therapy assistants (OES Occupation Code 31-2011). The opportunity cost of the time spent undertaking these activities would be calculated as follows:

Mean wages for occupational therapy assistants (national estimate) (OES, May 2014):	\$27.53 per hour[a]
Overhead cost per direct labor hour:	100 percent
Hours spent per employer:	5 hours
Opportunity Cost Per Employee:	\$27.53 * 2 * 5 = \$275.30

[a] Because all occupational therapy assistants employed throughout the United States will assume additional administrative tasks in response to the regulation, use of the mean is appropriate in this example.

Unpaid activities: HHS regulations may also impose administrative burdens on individuals (e.g., filling out additional paperwork for health care reimbursements) unassociated with their job. Unlike individuals employed in the labor market, those engaged in nonmarket labor activities are not compensated. As a result, the rationale for selecting a rate for valuing time spent performing such activities is less straightforward than for market labor.

As discussed earlier, economists often assume that the marginal value of an hour of uncompensated activity is equal to marginal compensation received. In other words, the opportunity costs of not working equal the value of the compensation the individual would have received if he or she chose to work. This value is generally estimated based on the post-tax wage an individual would have received for market work. This interpretation applies both to people employed in the labor force, who (in principle) could adjust their working hours and compensation, as well as to those out of the labor force, who presumably have chosen not to work because they value their time more highly than the rate at which they would be compensated.[70]

To estimate the hourly value of unpaid administrative tasks, analysts should apply the post-tax wage rate. This rate can be obtained by adjusting the pre-tax wage rates reported in the OES or NCS to remove taxes, which vary as a percentage of wages over time and across locations.[71]

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[69] See http://www.bls.gov/news.release/ecec.t01.htm, Table 1. Civilian workers, by major occupational and industry group (September 2015). Total benefits account for 31.4 percent of total compensation (wages and salaries plus benefits). To calculate the size of total benefits relative to wages and salaries, apply the following equation: 31.4/(100 – 31.4) = 45.8 percent.

[70] Analysts should also apply this approach when valuing time costs incurred by children or seniors (e.g., time spent at additional medical appointments), noting related uncertainties.

[71] National estimates of the Federal and State income taxes paid as a percentage of pre-tax income are difficult to obtain. The Internal Revenue Service (IRS) provides detailed reports of total Federal income tax collected relative to adjusted gross income; however, these data exclude State taxes (see, for example, "Individual Income Tax Rates and Tax Shares" at https://www.irs.gov/uac/SOI-Tax-Stats-Individual-Income-Tax-Rates-and-Tax-Shares).

To estimate the tax rate, including both Federal and state taxes, analysts should use data on household income before and after taxes collected in the CPS, a joint effort by the U.S. Census Bureau (Census) and BLS. The CPS collects data from a nationally-representative sample of 60,000 households on a monthly basis.[72] The Census maintains a tool called the "CPS Table Creator," which allows analysts to create customized data tables.[73] It provides both mean and median income; as with wage rates, which central tendency estimate analysts should use will depend on the specific characteristics of the rule.[74] Figure 4.2 provides an example calculation of the value of time spent on unpaid administrative tasks.

For both paid and unpaid work time, the representativeness of the wage and tax rate estimates is likely to be uncertain. Where plausible alternative estimates exist, analysts should test the sensitivity of their results to these assumptions (see Chapter 6), particularly if the alternative estimates significantly affect the analytic conclusions.

Materials: Materials used to complete administrative activities may include office supplies or other items. Generally, analysts should obtain cost estimates from readily-available office supply catalogs or websites and courier services (e.g., the U.S. Postal Service, Federal Express, United Parcel Service, DHL). In addition, the rule may generate a need for records storage, either electronically or on paper. If a substantial amount of data must be stored, analysts should consider the costs of electronic file storage and backup, rent for additional storage space, or the cost of filing cabinets or boxes.

Travel: Administrative costs may include travel, particularly where the new rule creates a need for meetings or training activities. The U.S. General Services Administration (GSA) provides per diem travel rates for lodging and meals.[75] For air travel, plane fares can be obtained using internet travel search engines. For travel by car, the Internal Revenue Service (IRS) publishes reimbursement rates for mileage.[76] The mileage rate can be applied to estimates of miles traveled obtained from internet websites providing travel directions. Analysts should also include travel time, as discussed earlier.[77]

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[72] Household tax rates are appropriate because ideally individuals should make decisions based on the tax rates they actually pay.

[73] To estimate mean or median household income before taxes, under "Data Options" select the relevant calendar year and get a count of "Persons-All." Next, "Define Your Table" by selecting "Household Income – Alternative" as a row variable. Under the "Statistics" section, in the subsection called "Additional numeric variable statistics" choose "Household Income-Alternative" and "Mean" or "Median." In the "Income Definition" section, select "Customize your own income definition" and then select "1. Earnings (wages, salaries, and self-employment income)" and "19. Federal Earned Income Credit." For household income after taxes, follow the same steps and add the following additional selections in the customized income definition: "20. Federal Income Taxes after refundable credits except EIC," "21. State income taxes after all refundable credits," and "22. Payroll taxes (FICA and other mandatory deductions)." For 2014 (select 2015 as the most recent year of data), median pre-tax household income ($53,000) minus post-tax income ($44,599) and divided by median pre-tax income results in a median tax rate of 16 percent. (To access the CPS Table Creator, see http://www.census.gov/cps/data/cpstablecreator.html).

[74] As with wage rates, ideally, analysts would use estimates of the marginal tax rate (i.e., the tax rate applied to the last dollar of income earned) to make this adjustment, rather than the average tax rate paid for all income. While data on the distribution of marginal tax rates paid by the U.S. tax filers are available from the IRS, they only include Federal taxes; excluding State or other taxes. Thus, analysts should use the CPS data, even though it provides mean or median, rather than marginal rates, because it includes both Federal and State taxes.

[75] See GSA's website "Per Diem Rates Look-up" at http://www.gsa.gov/portal/category/100120.

[76] See IRS's website "Standard Mileage Rates" at http://www.irs.gov/Tax-Professionals/Standard-Mileage-Rates.

[77] See DOT (2015b) for recommended adjustment factors for the hourly estimates of value of time spent traveling, for different types of travel (available at: http://www.dot.gov/office-policy/transportation-policy/guidance-value-time). That document provides a detailed discussion of the theoretical and empirical basis for these adjustment factors.

FIGURE 4.2. SAMPLE CALCULATION OF THE VALUE OF TIME SPENT ON AN UNPAID ADMINISTRATIVE TASK

Assume a proposed rule will result in five additional hours each year of administrative work for a subset of affected individuals (working and non-working adults, children, and seniors) in the United States. The opportunity cost of the time spent undertaking these activities would be calculated as follows:

Median wages, all occupations (OES, May 2014)	= $17.09 per hour[a]
Median household tax rate (CPS, 2014 data)	= 16 percent[a]
Hours spent per individual	= 5 hours
Opportunity cost per individual	= $17.09 * [1-0.16] * 5 = $71.78

[a] In this instance, the distribution of income among the subset of the population subject to the regulation may not be representative of the U.S. income distribution. Therefore, the median may represent the best central tendency estimate of wage and household tax rates for affected individuals.

4.2.2 CAPITAL AND OPERATIONS AND MAINTENANCE COSTS

Regulated entities may also need to purchase and operate new equipment to comply with regulatory requirements. For example, they may need to purchase new computers and software, change equipment or maintenance schedules at a production facility, or adopt other new technology. In this section, we describe methods for estimating such costs.

Equipment and other capital components: Capital costs generally refer to the reallocation of resources needed to purchase and operate additional equipment or other inputs that are not immediately consumed in the production process. [78] Typical capital costs may include, for example: purchasing computers and software to support administrative tasks; or installing or retrofitting new equipment associated with the production of food, drugs, or other goods. Some regulations may lead to capital expenditures to acquire buildings or land.

Generally, analysts use market data to estimate the price of purchasing and installing such equipment. These data may be obtained through interviews, literature reviews, review of online merchandise catalogues, or other sources. In some cases, the cost of the equipment may include installation costs and it will not be necessary to separately estimate the costs of associated labor. Otherwise, labor costs should be estimated in terms of the fees paid to licensed installers or, if the work is completed in-house, using the approach for valuing paid time described above. Information describing the useful life of the equipment is also necessary to determine whether the equipment must be replaced during the time period of the analysis. Finally, a side cost often associated with installation is the temporary shutdown of operations (i.e., forgone revenues net of avoided variable operations and maintenance (O&M) costs). In many cases these costs are minimized by installing or retrofitting equipment during regular downtimes (e.g., for maintenance).

Operations and maintenance costs: O&M costs include the annual costs of labor, utilities, and other resources required to operate and maintain capital equipment, as well as other expenditures that do not involve the purchase of a capital asset. Typical O&M costs include labor costs (discussed earlier); electricity and other utilities; replacement parts; raw materials and other inputs to production. O&M costs may be variable, in that

[78] Note that capital costs described in this section should not be confused with the fixed overhead component of the overhead rate used to estimate the value of time (see Table 4.2). In the latter case, overhead costs are used as a proxy to estimate the value of time. This section, in contrast, describes the valuation of additional equipment or other goods that may be necessary to implement a proposed regulation. Where an entity purchases new equipment (e.g., hard drives) to store compliance information and shifts staff resources (without hiring additional staff) to undertake administrative tasks, time cost and capital cost should be summed (they are not duplicative).

they fluctuate with production levels, or fixed, where the costs are not tied to production levels.[79] Again, analysts generally use market data to estimate such costs.

For both capital and O&M costs, analysts must be careful to estimate incremental costs. For example, if a firm needs to purchase new and improved equipment to replace current machinery (or the machinery they would purchase during their next scheduled turnover), the incremental costs of the rule include only the costs above and beyond those associated with the equipment the firm would have otherwise purchased. Therefore, data are required on the cost and useful life of both the existing equipment and the newer technology needed to comply with the regulation.[80]

4.2.3 MEDICAL COSTS

Medical costs may be relevant to either the benefit or cost calculations depending on the characteristics of the regulation. As noted in Chapter 2, costs are generally the inputs and benefits are the outputs or outcomes of a policy. Thus if increases or decreases in medical costs are part of the implementation of the requirements (i.e., an input), they should be counted on the cost-side of the equation. If they are part of the intended outcome, then they should be included in the benefit calculation, taking care to avoid double-counting with other benefit measures. For some rules, whether medical costs or savings should be counted as a “cost” or “benefit” will be uncertain, and analysts will need to discuss where they are counted in documenting the analysis. Medical costs generally should be presented as a separate line item in the calculations so their treatment is clear.

The appropriate calculation of medical costs in benefit-cost analysis is an area where more work is needed, because of the substantial distortions introduced by regulation of the health care sector and the effects of government and private insurance reimbursement policies. These distortions drive a wedge between market prices and opportunity costs, which make estimation difficult. Comparison across studies suggests that different approaches can lead to noticeably different results (e.g., Bloom et al. 2001; Akobundu et al. 2006; Larg and Moss 2011), but there is no established set of recommended best practices. In addition, much of the available data were developed to support reimbursement decisions and are not necessarily appropriate for estimating opportunity costs. HHS is now undertaking a project to further explore this issue; in the interim analysts should follow the general approach described below and discuss associated uncertainties.

When benefits consist of mortality and morbidity risk reductions, as discussed in Chapter 3, only some types of costs should be added to the estimates of individual WTP used for valuation. More specifically, the value per statistical life (VSL) estimates used to value mortality risk reductions, and the WTP estimates used to value morbidity risk reductions (including the estimates of monetized QALYs) used as proxies when suitable WTP estimates are not available), may include costs borne by the affected individuals. They presumably reflect the effect of the risk reductions on the activities the individual undertakes (including the allocation of both work and non-work time), and may also reflect out-of-pocket costs. Hence to avoid double-counting, savings in medical costs are generally not added to these benefit values. The one exception is when the costs in the absence of the regulation would be borne by third parties, in which case any savings in resource costs (excluding transfers) may added.

When a regulation imposes costs on the health care sector, for example by establishing or changing requirements for treatment, then medical costs may be included in the cost analysis. As a simple illustration, assume that a regulation requires monitoring the health of all workers exposed to contaminants while cleaning up after a natural disaster. The costs of the regulation would include the incremental cost of the medical

[79] For example, variable costs, such as raw materials used as inputs to production, will rise or fall with production levels. Fixed costs, such as rent or utilities, do not vary with production levels in the near-term.

[80] Analysts should consider whether compliance costs may decrease over time as regulated entities gain experience with the new regulation. A significant body of literature related to the operation and management of industrial processes suggests that the per-unit cost of producing or using a given technology declines as experience with that technology increases over time (see Baloff 1971, Dutton and Thomas 1984, and Epple et al. 1991). For a review of the literature measuring the “learning rate” for different industries and technologies, see Auerswald et al. (2000).

monitoring. The health benefits that result from earlier detection and treatment (than in the absence of such monitoring) would be valued using the approaches discussed in Chapter 3.

Analysts must also consider whether the cost assessment requires prevalence-based or incidence-based per case estimates. The former typically reflect the average costs of all cases in a given year, and may be appropriate for short-lived effects, such as acute health conditions or time-limited monitoring and treatment programs (e.g., in the immediate wake of a natural disaster). Incidence-based estimates instead track or model the lifetime costs per case, and are desirable when the regulation affects the incidence of chronic conditions or longer-term monitoring and treatment programs. In these cases, costs are likely to fluctuate over time, and extrapolating lifetime costs from prevalence-based estimates may understate or overstate actual costs. Incidence-based estimates that consider the entire, multi-year progression of the disease may be preferable. The appropriate measure will depend on the data available as well as the nature of the health effect.

Analysts will need to review the existing literature for recent studies of the specific health effects and types of costs needed for a particular regulatory analysis. Akobundu et al. (2006) and Larg and Moss (2011) provide useful overviews of the characteristics and limitations of different measurement approaches applied by researchers. Lund et al. (2009) provide a comprehensive inventory of relevant data sources. In addition, analysts should consider contacting health economists who focus on the conditions of interest, such as technical experts at the Centers for Disease Control and Prevention, academic institutions, or nonprofit research organizations. The series of articles included in Yabroff et al. (2009) also provide useful information.

In summary, estimating medical costs requires substantial professional judgment; the appropriate approach will depend on the characteristics of the practices affected by the regulation as well as the available data. Analysts are encouraged to work with subject matter experts if they are unfamiliar with methods used to estimate medical costs or with the particular health effect of interest.

4.2.4 GOVERNMENT IMPLEMENTATION COSTS

Government entities may also incur costs, either as an implementing or regulated entity. For example, a regulation may impose new review, reporting, and record keeping requirements on State or local government entities responsible for recording vital statistics, such as births and deaths. In this example, the HHS may incur implementation costs related to developing guidance, conducting training, and increasing enforcement. Likewise, State and local governments may incur compliance costs to train staff, adjust their electronic databases and reporting systems, and alter how they store information.

If the government is involved in implementing the regulation, the costs to the agency represent an opportunity cost of the regulation, as do similar costs imposed on industry, even if no new staff are hired. The effort undertaken to implement the regulation would otherwise be spent on other productive tasks. Thus, these costs should be counted in the analysis, using the methods discussed above. Information included in internal budget estimates, such as full-time equivalent labor needed for the program or requests for capital expenditures, are useful sources of data for these cost estimates.

If the government is the subject of the regulation, estimating related costs also follows the same approaches described elsewhere in this chapter. If grants or other funding are provided by HHS to support implementation of the regulation by industry or others, these funds are transfers and should not be included as costs, assuming they have no behavioral impacts that could affect the estimates of national net benefits. However, the amount of the funding may serve as a proxy estimate of the compliance costs imposed by the rule, to the extent that related costs are fully covered.

4.3 ESTIMATING MARKET-LEVEL IMPACTS

The preceding sections assume that the proposed regulation will not significantly affect the quantity of goods produced (e.g., a new regulation resulting in increased costs to electronically store and transmit data related to certain medical procedures will not affect the quantity of procedures performed). When the regulation is anticipated to affect the quantity of goods produced, a more precise estimate of social costs would involve estimating changes in consumer and producer surplus (see Appendix B) using partial or general equilibrium models.

Where a single market or a small number of unconnected markets are affected, partial equilibrium analysis provides a useful tool for estimating welfare changes. Analysts use information about the quantity and price of goods produced without the regulation, compliance costs, and elasticities of supply and demand to estimate the equilibrium output with the regulation and net changes in consumer and producer surplus (see Appendix B and Boardman et al. 2011).[81] In addition to providing a more precise estimate of welfare changes, a partial equilibrium model also provides insight into who bears the cost of the regulation. Such information may be important if analysts anticipate the regulation will have significant distributional impacts (see Chapter 7).[82]

WHEN SHOULD ANALYSTS USE PARTIAL OR GENERAL EQUILIBRIUM MODELS?

Analysts should consider employing partial or general equilibrium models when changes in consumer and producer surplus are likely to significantly affect the analytic conclusions. For example, such effects might be important if large sectors of the U.S. economy are affected or if impacts are likely to be measurable at a national scale (e.g., relative to U.S. gross domestic product, GDP). In most cases, estimating compliance costs is a sufficient proxy for changes in surplus.

Where multiple, interconnected markets are affected, or substantial international effects are anticipated, analysts might consider using computable general equilibrium analysis to estimate impacts. Such modeling may also be useful when a regulation is part of a larger suite of regulations that may have economy-wide, interactive effects. These models measure shifts in production and consumption resulting from compliance costs. In addition, they estimate how shifts in quantity or price in one market affect related markets. General equilibrium models are complex and generally require a significant amount of data to capture the effects of a regulation (see Berck and Hoffman 2002 and Lofgren et al. 2002). Such analysis requires working with a pre-existing model developed by one of several academic, government, or other institutions.[83]

[81] Because compliance costs serve as the basis for changes in the supply curve, analysts should not combine separate estimates of total compliance costs with estimates of changes in surplus. Adding these cost estimates together would result in double-counting.

[82] For example, for products where consumer demand is relatively inelastic, producers may have greater ability to pass compliance costs on to consumers in the form of higher prices.

[83] Examples of computable general equilibrium models used by Federal agencies to estimate impacts to the U.S. economy include the Global Trade Analysis Project (GTAP) model, the USAGE model, the Intertemporal General Equilibrium Model, and EMPAX-CGE.

Chapter 5

Account for Timing

The costs, benefits, and other impacts of regulations often accrue over several years, requiring that analysts take into account how affected individuals value impacts that occur in different time periods. In addition, RIAs generally involve applying data that reflects past rather than current price levels. Thus analysts must both inflate prices from prior years to the same dollar year, and discount future impacts back to the base year in which the regulation is first implemented.[84] Carrying out these steps involves distinguishing between inflation and real changes in value, and understanding how to appropriately account for time preferences. Below, we first discuss the underlying concepts and basic approach, then describe how to adjust for inflation, calculate discounted present values, and determine impacts on an annualized basis.

5.1 BASIC CONCEPTS AND APPROACH

Consider the four streams of payments in Table 5.1. If they represent the net benefits of different policy options in each year, how might we choose among them? Options A, B, and C sum to the same total over the 10 year period, but the net benefits vary across years. Under Option A, costs substantially exceed benefits for two years after which benefits exceed costs; under Option B, costs also initially exceed benefits but by lesser amounts and for a longer period; under Option C, benefits exceed costs by the same amount in all years. Option D sums to a smaller total with net benefits that decline over time. Comparing such streams of payments, regardless of whether they represent costs, benefits, or net benefits, requires (1) understanding whether they include the effects of inflation and (2) addressing time preferences through discounting. In combination, considering these issues allows us to determine which option is preferable.

TABLE 5.1. COMPARING UNDISCOUNTED ANNUAL NET BENEFITS

YEAR	0	1	2	3	4	5	6	7	8	9	TOTAL
Option A	**($2,000)**	**($1,000)**	$200	$300	$400	$500	$600	$600	$700	$700	$1,000
Option B	**($600)**	**($500)**	**($400)**	**($300)**	$100	$200	$300	$600	$700	$900	$1,000
Option C	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$1,000
Option D	$200	$200	$200	$50	$50	$50	$50	$50	$50	$0	$900

The first question is whether values are measured in real or nominal dollars. Observed prices are measured in nominal (current-year) dollars. Because these prices may be affected by economy-wide inflation, values in different years are not necessarily comparable. If there is inflation, the quantity of goods one can buy for $1.00 decreases over time. Real (constant or inflation-adjusted) dollars net-out the effect of inflation so that dollars have equal purchasing power over time and are comparable across different periods.

To avoid misleading comparisons, regulatory analyses should always be conducted in constant (real, inflation-adjusted) dollars.[85] This approach has the advantage of allowing analysts to avoid the difficult task of attempting to project future inflation rates. As discussed in more detail in section 5.2, all values should be first converted to the same year dollars, then the analysis should be conducted in real dollars from that point forward. For example, a regulatory analysis prepared in 2015, which projects benefits and costs over the next 10 or 20 years,

[84] As discussed in more detail later, the dollar year is likely to differ from the base year used for discounting.

[85] For the remainder of this discussion, we assume that the values in Table 5.1 are undiscounted and expressed in real terms.

may be conducted in constant 2014 dollars. Generally, a dollar year should be selected that is reasonably close to the current year.[86]

The second question is how to weight real benefits and costs that accrue in different time periods. There are two interrelated reasons why values are not likely to be weighted equally over time. One is individual time preferences; people generally prefer to receive benefits as soon as possible and to defer costs. The other is opportunity costs; resources received today can be invested to yield a positive return while resources expended are no longer available for investment.[87]

Analysts account for the effects of timing by discounting future impacts to the *base* year of the analysis. This base year commonly reflects the first year in which the regulation is implemented, and is likely to differ from the *dollar* year selected for the analysis. For example, an analysis conducted in 2015 may express all values in 2014 dollars. However, if the rule will not be implemented until 2017, the analysts may use 2017 as the base year for discounting. The dollar year and the base year must be clearly identified throughout the analysis.

Although there are conceptual differences between a discount rate and an interest rate, they are closely related. An interest rate is the market rate at which money can be borrowed or loaned, and results from the interaction between market participants' willingness to save and demand for borrowing. The discount rate reflects preferences for receiving benefits or bearing costs at different dates, which may be influenced by the opportunity costs imposed by regulations or by similar actions that divert resources from other investments or consumption. In practice, discount rates are often based on market interest rates.

As in the case of prices, care must be taken to distinguish between nominal and real discount rates. Because regulatory analyses are conducted in real dollars, a real discount rate must be applied. Below, we first discuss how to adjust for inflation. Section 5.3 then discusses discounting in more detail, and Section 5.4 describes how to convert discounted amounts to annualized dollars.

HOW SHOULD ANALYSTS ACCOUNT FOR THE EFFECTS OF TIMING?

Analysts should first select a common *dollar* year, and inflate all unit values to that year. They should then calculate the benefits, costs, and net benefits expected to accrue in each future year of the analysis, report the undiscounted stream of benefits and costs, and report their present value applying discount rates of 3 and 7 percent. Analysts should also report annualized values (calculated using each discount rate). The *base* year used when calculating present values should be the year in which the regulation is initially implemented, and may differ from the dollar year.

5.2 ADJUSTING FOR INFLATION

In regulatory analysis, analysts often work with data from many different time periods; an analysis conducted this year is likely to rely on unit cost and benefit data collected in several previous years. Adjusting for inflation involves using an index to convert all dollar values to the same year dollars. Indices commonly used to reflect economy-wide trends are the Consumer Price Index (CPI), and the gross domestic product (GDP) implicit price deflator. Because the CPI is more easily accessible, it is more frequently applied.[88] In general, the two approaches yield similar estimates of the inflation rate.

[86] A year prior to the current year is generally used as the dollar year because the rate of inflation for the current year is not yet known.

[87] The two reasons are related. When real interest rates are positive, individuals can purchase more goods and services if they postpone those purchases by saving more or borrowing less. To maximize utility (well-being), they should allocate their spending over time such that their preference for incremental current over future spending equals the interest rate. Real interest rates are typically positive because individuals require compensation for deferring consumption.

[88] As discussed in Chapter 8, the GDP deflator must be used in preparing the accounting statement required under OMB *Circular A-4*. It is also used to determine the threshold for conducting analyses under the Unfunded Mandates Reform Act as discussed in Chapter 7 (see, for example, HHS 2015). However, within the analysis itself, the CPI (or more specialized indices) may be used instead of the GDP deflator to adjust benefits and costs to the same year dollars.

Other, more specialized indices are also available that reflect price trends in particular market segments (such as producer prices or medical services) or in particular geographic areas. In this section, we focus on the CPI and GDP deflator, since these are the indices most commonly used in regulatory analysis. However, in some cases analysts may instead apply more specialized indices. The inflation index or indices used, and the rationale for applying them, must be clearly documented in the RIA.

The CPI is developed by the Bureau of Labor Statistics within the U.S. Department of Labor. It measures the average change over time in the prices paid by urban consumers for a market basket of goods and services. (According to the Bureau of Labor Statistics, these urban consumers represent about 87 percent of the U.S. population.[89]) The CPI is based on detailed information on actual expenditures by a statistically-representative sample of individuals and families, including all consumption goods and services.

The CPI website includes an inflation calculator (http://www.bls.gov/data/inflation_calculator.htm) that can be easily used to convert values to the same year dollars, based on purchases of all goods and services nationally. If an analyst prefers to directly apply the index values from the CPI tables (for example, including these values in a spreadsheet used to calculate benefits and costs), the index values must be converted to reflect the rate of change, expressed as a proportion or percentage. For example, if the analyst wishes to inflate a value from dollar year “a,” in which the index was 120, to a dollar year “b,” in which the index was 140 (a 20 point difference), the increase would be (20/120) * 100 = 17 percent.[90] Thus a unit cost of $100 in year “a” dollars would become $117 if expressed as year “b” dollars.

More generally, to inflate a value from year “a” to year “b,” the percentage change is calculated as:

Percent inflation (CPI) =

$$((CPI_{year\ b} - CPI_{year\ a}) / CPI_{year\ a}) * 100$$

The GDP deflator is instead based on the value of all goods and services produced within the U.S. economy; it also can be calculated for subsectors of the economy. It is developed by the Bureau of Economic Analysis in the U.S. Department of Commerce, and includes personal consumption, domestic investment, net exports, and government consumption and investment.[91] It is not derived from a market basket of goods; rather it changes depending on investment and consumption patterns.

The GDP deflator is provided in Table 1.1.9 of the National Income and Product Accounts, which can be accessed through the Bureau of Economic Analysis website.[92] Again, as in the case of the CPI, the index values need to be converted to a proportional or percentage change to be applied in the analysis. This conversion follows the same formula as provided above for the CPI.

5.3 DETERMINING PRESENT VALUES

Once all unit benefits and costs are converted to the same dollar year (i.e., to constant dollars) and the year in which they occur is identified, the next step is to calculate their discounted present value. This value indicates how much dollars paid or received at a later time are worth in the base year (i.e., the year in which the regulation is first implemented), given time preferences and opportunity costs as discussed earlier.[93] For

[89] This and other basic information on the CPI is available at http://www.bls.gov/cpi/cpifaq.htm.

[90] The change can also be expressed as a multiplier, applying the formula $CPI_{year\ b}$ / $CPI_{year\ a}$ (140/120 = 1.17 percent in the example). In spreadsheet analysis, converting the proportion into a percentage is not necessary; the analyst may simply enter the proportion and multiply the year “a” value by the result.

[91] A glossary of related terms is available at: http://www.bea.gov/glossary/glossary.cfm; more information on the underlying concepts and methodology is available at: http://www.bea.gov/methodologies/.

[92] To access this table: (1) click on the “Interactive Data” tab at the top of http://www.bea.gov/; (2) select “GDP & Personal Income” under “National Data;” (3) click on “Begin Using the Data;” (4) under “National Income and Product Account Tables,” click on Section 1, and select Table 1.1.9, “Implicit Price Deflators;” (5) click on the “Options” icon to choose the desired time period and to indicate annual as the frequency, then select “Update” to regenerate the table.

[93] In some cases, regulated entities may begin to respond to the regulation before it becomes effective, and related costs, benefits, and net benefits will need to be carried forward to the base year rather than discounted. In this case, their value will increase rather than decrease between the time when they are incurred and the base year.

regulatory analysis, the OMB guidance in *Circular A-4* (2003) requires agencies to report the results of their analyses applying discount rates of three and seven percent per year.[94] The use of two rates reflects uncertainty about whether regulation is likely to displace investment or consumption.[95] In a simple theoretical model, investment- and consumption-based discount rates would be equal, but in reality distortions such as taxes lead to differences.

The seven percent rate is intended to reflect the opportunity costs associated with displacing private investment, and was based on the estimated average before-tax rate of return to private capital in the U.S. economy at the time when the OMB guidance was developed. The three percent rate is intended to reflect the opportunity costs associated with displacing consumption (often referred to as the marginal "social rate of time preference"), and was based on the before-tax rate of return on long-term government debt to approximate the interest paid on savings. This approach assumes that the savings rate represents the average by which consumers discount future consumption. Both are real rates, consistent with the use of real dollars when estimating benefits and costs.

The formulae for calculating present values are provided in Figure 5.1.

FIGURE 5.1. CALCULATING PRESENT VALUES

If:

- PV = present value as of the base year
- FV_t = future value in the year (t) when the benefit or cost accrues
- NPV = net present value of benefits and costs combined across all time periods
- r = the discount rate
- t = the number of years in the future (measured from the base year) when the cost or benefit accrues
- n = the number of years included in the analysis

Then the discount factor for costs or benefits that accrue at the end of year t is:

$1/(1+r)^t$

The present value of a future cost or benefit that accrues in year t is:

$PV = FV_t\ (1/(1+r)^t\ )$

The net present value for a stream of future benefits and costs is:

$NPV = V_{t=0} + (FV_{t=1}/(1+r)\ ) + (FV_{t=2}/(1+r)\ ^2) + (FV_{t=3}\ /(1+r)\ ^3)...(FV_{t=n}/(1+r)\ ^n)$

Most spreadsheet programs automate these calculations, as do many calculators. In Excel, the function is NPV(r, [range or list of cells with flows ordered from "now" to the last period]).[96] Financial calculators typically have an NPV function into which you can enter a stream of costs, benefits, or net benefits as well as a discount (interest) rate. While in Excel r should be entered as a decimal (e.g., 0.03 if the discount rate is three percent), in many calculators r instead must be entered as a percentage (e.g., 3). The Excel function also has some optional arguments, such as whether the payments occur at the start or end of each period. While the end of the period

[94] While OMB allows agencies to apply other rates if justified, in practice agencies usually apply only the three and seven percent rates for intra-generational impacts. Discounting inter-generational impacts (for policies such as those addressing climate change or radioactive waste storage) raises several difficult issues related to forecasting future preferences and opportunity costs as well as inter-generational equity. HHS analysts rarely need to address these concerns because most HHS analyses cover shorter time periods; i.e., 10 to 20 years as noted earlier in this this guidance. OMB *Circular A-4* (2003) provides more discussion of these issues.

[95] On occasion, it may be informative to estimate the internal rate of return, which is the discount rate at which benefits equal costs (i.e., the net present value is zero). Calculating the internal rate of return is generally not useful for selecting among regulatory alternatives, however. A policy may have more than one internal rate of return if net benefits change from positive to negative (or vice-versa) more than once over the time period addressed. In addition, as is the case for both benefit-cost and cost-effectiveness ratios, the internal rate of return is not sensitive to scale. It does not indicate the amount by which benefits exceed costs, and hence does not provide information on which policy maximizes net benefits when policies differ in size.

[96] Excel also provides a present value function [PV(r, n, payment per period)] that is useful when the values are the same in each period.

is the Excel default, analysts often instead assume that payments occur at the beginning of each period, which means that the impacts in the base year (year "0" in the examples) are not discounted. In this case, a value of "1" must be entered into the Excel formula under "type," to change the default from the end to the beginning of each period.[97]

As discussed in Chapter 2, benefits and costs generally should be assessed over a 10-to-20 year period, consistent with the OMB guidance, unless the policy terminates sooner. Analysts should select a period that is adequate to encompass the time needed for the regulation to become fully effective, without requiring extrapolation so far into the future that predicting impacts become highly speculative given changes in the population, economy, technology, and other factors. Impacts further in the future often add relatively little to the present value of benefits and costs, given the effects of discounting, and are unlikely to alter the policy implications of the analysis. However, longer time periods may be considered if clearly justified.

We can use the streams of undiscounted net benefits in Table 5.1 to provide an example of this process. First, consistent with the OMB guidance in *Circular A-4*, analysts should present the stream of undiscounted costs, benefits, and net benefits (as illustrated for net benefits in Table 5.1), to aid decision-makers in understanding the timing. Presenting these graphically is often useful, as illustrated in Figure 5.2 for Option A from Table 5.1.

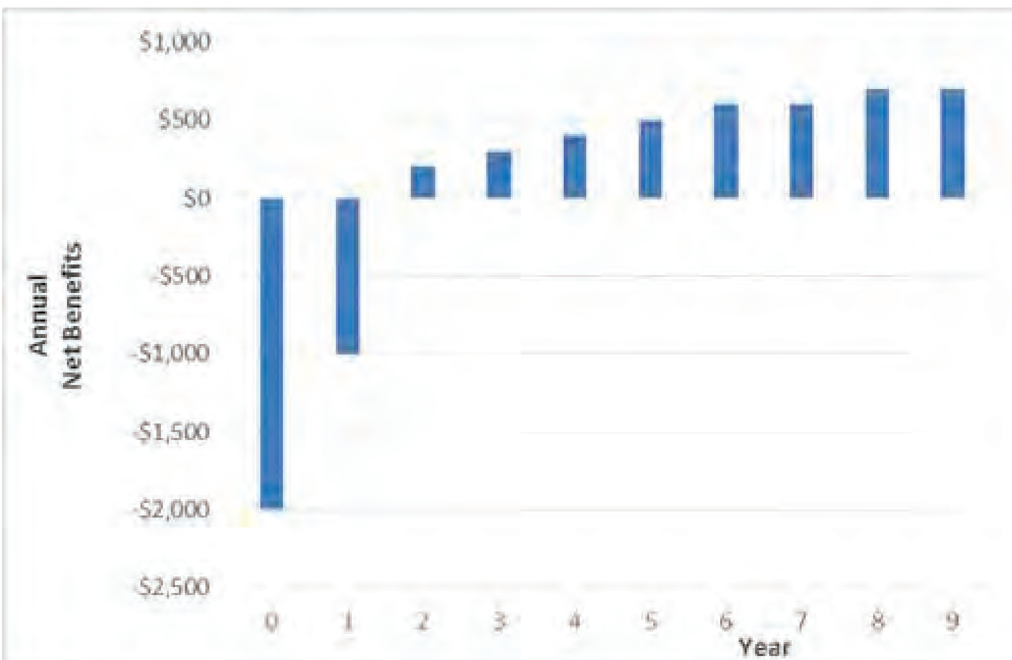

FIGURE 5.2. EXAMPLE PRESENTATION OF UNDISCOUNTED NET BENEFITS

Second, OMB requires that the results be presented using different discount rates, as illustrated in Table 5.2. This table presents the same four streams of net benefits as Table 5.1, undiscounted as well as discounted applying rates of the three and seven percent. Calculating present values makes it clear that the preferred option depends on the discount rate. Without discounting, Options A, B, and C all appear preferable to Option D. Discounted at a three percent rate, Option C is the best option. If the discount rate is seven percent, then Option D becomes best. At a seven percent rate, the net benefits of Option A also become negative. Thus at this rate, Option A would not be preferred to the "no action" baseline even if it were the only option being considered, since its costs exceed its benefits.

[97] While typically impacts incurred in the base year are not discounted, assuming payments occur at the beginning of each period, for some regulations analysts may find that it is more appropriate to assume end-of-period payments. In that case, base year impacts should be discounted and the Excel default assumption is appropriate. In the RIA, analysts should report the timing assumption used and the same assumption should be applied throughout the analysis.

TABLE 5.2. COMPARING DISCOUNTED NET BENEFITS

YEAR	0	1	2	3	4	5	6	7	8	9	NPV
Undiscounted											
Option A	($2,000)	($1,000)	$200	$300	$400	$500	$600	$600	$700	$700	$1,000
Option B	($600)	($500)	($400)	($300)	$100	$200	$300	$600	$700	$900	$1,000
Option C	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$1,000
Option D	$200	$200	$200	$50	$50	$50	$50	$50	$50	$0	$900
Discounted to Year "0" at 3 Percent											
Option A	($2,000)	($971)	$189	$275	$355	$431	$502	$488	$553	$536	$358
Option B	($600)	($485)	($377)	($275)	$89	$173	$251	$488	$553	$690	$506
Option C	$100	$97	$94	$92	$89	$86	$84	$81	$79	$77	$879
Option D	$200	$194	$189	$46	$44	$43	$42	$41	$39	$0	$838
Discounted to Year "0" at 7 Percent											
Option A	($2,000)	($935)	$175	$245	$305	$356	$400	$374	$407	$381	($292)
Option B	($600)	($467)	($349)	($245)	$76	$143	$200	$374	$407	$490	$28
Option C	$100	$93	$87	$82	$76	$71	$67	$62	$58	$54	$752
Option D	$200	$187	$175	$41	$38	$36	$33	$31	$29	$0	$770

As demonstrated by Table 5.2, the choice of a discount rate can have a significant effect on the estimated net benefits. Whether the discount rate will affect the conclusions of the analysis will depend on the pattern of benefits and costs over time for each alternative considered. The option that provides the largest net benefits will depend on the magnitude of the impacts and their timing, as well as on the discount rate. Generally, the decision rule is that if only one policy is considered, then the policy should be implemented if the present value of net benefits is greater than zero. For regulatory analyses, which should consider multiple options (as discussed in Chapter 2 of this guidance), the option that is preferable in terms of economic efficiency will be the option with the largest net benefits, as long as the net present value is greater than zero.

5.4 ANNUALIZING IMPACTS

For regulatory analyses, OMB *Circular A-4* (2003) also requires that analysts present benefits, costs, and net benefits on an annualized basis to facilitate comparisons across analyses that cover different time periods. The annualized value of a stream of benefits, costs, or net benefits is the constant annual amount that, if maintained for the same number of years as the initial stream, has the same present value. In other words, annualization spreads the costs, benefits, or net benefits equally over the time period assessed, taking the discount rate into account. The concept is similar to amortization of a loan, in which the principal and interest are paid through a series of constant payments.

The formula for annualization is provided in Figure 5.3; the expression in brackets transforms a value into an annuity of n years at a discount rate r. Note that applying this formula requires first estimating the present value, following the formulae in Figure 5.1 as discussed in the preceding section.

FIGURE 5.3. CALCULATING ANNUALIZED VALUES

If:

- PV = net present value of costs, benefits, or net benefits
- r = the discount rate
- n = the number of years included in the analysis
- AV = annualized value

The annualized value is:

$$AV = PV * [(r * (1 + r)^n) / ((1 + r)^n - 1)]$$

Once a present value is calculated, it can be easily converted to an annualized value using spreadsheet software or a financial calculator. In Excel, the function is PMT (r, nper [number of periods], and PV). Because the PMT function is designed to calculate loan payments, it will provide a value with the opposite sign of the present value; simply reversing the sign will provide the correct amount for the purpose of regulatory analysis. OMB's 2011 Regulatory Impact Analysis: Frequently Asked Questions provides more detailed, step-by-step guidance on these calculations.

The annualized value is an alternative method for expressing the net benefits; the ranking of policies by annualized value will be the same as the ranking by present value net benefits when estimated over the same time period. To illustrate, in Table 5.3 we provide the results for the same streams of net benefits as assessed in Table 5.2. The conclusions are the same: Option C has the largest annualized value under a three percent rate; while Option D has the largest annualized value under a seven percent rate. If, however, these options were implemented over different time periods, the results could vary.

TABLE 5.3. COMPARING ANNUALIZED NET BENEFITS

OPTION	ANNUALIZED
Undiscounted	
Option A	$100
Option B	$100
Option C	$100
Option D	$90
Discounted at 3 Percent	
Option A	$41
Option B	$58
Option C	$100
Option D	$95
Discounted at 7 Percent	
Option A	**($39)**
Option B	$4
Option C	$100
Option D	$102

Because annualization provides a different perspective than the estimate of net present values, both annualized and present values should be reported in the RIA along with information on the time period over which these measures are calculated. The annualized value measures the average flow over the years included; the net present value measures the total. Annualized estimates are also needed to complete the accounting statement that must be submitted to OMB along with the RIA, as discussed in more detail in Chapter 8.

Chapter 6

Address Uncertainty and Nonquantifiable Effects

Any analysis involves uncertainties, including difficulties related to quantifying some potentially important effects. The challenge for the analyst is to determine how to best assess or quantify these uncertainties to support decision-making. The goal is to ensure that decision-makers and other stakeholders understand the extent to which key uncertainties – in the data, models, and assumptions – affect the main analytic conclusions.

For example, if the agency's best estimates suggest that benefits exceed costs for a particular regulatory option, how likely is it that this conclusion would be reversed given uncertainty about the magnitudes of the quantified effects and the potential impact of nonquantified effects? Might these uncertainties affect the relative rankings of the policy options? Answering these questions requires quantifying impacts to the greatest extent possible, and identifying key uncertainties and exploring them in both quantitative and qualitative terms. Over time, analysts should work to reduce these uncertainties and minimize the types of effects that cannot be quantified, by anticipating future analytic needs and investing in research that will be useful across a variety of regulatory analyses.

This chapter discusses strategies for characterizing the uncertainty in quantified effects as well as the potential impacts of nonquantified effects. It focuses on the benefit-cost analysis, as discussed in the prior chapters, but the approaches it describes are applicable to the supplemental analyses discussed later in this guidance as well. As with other analytic components, the uncertainty analysis is often iterative; the initial analysis may lead to decisions to conduct more research or to change the assumptions used, and perhaps to explore other policy options.

Although the assessment of uncertainty (including nonquantified effects) may be described along with the analytic methods when documenting the RIA (see Chapter 8), it is often helpful to summarize key uncertainties in a separate section. For example, the chapter describing the benefits analysis could first describe the analytic approach, then present the results, and conclude by discussing uncertainty and its implications. The executive summary, and the chapter that compares costs to benefits, could consolidate the most important findings from the individual chapters and describe how the uncertainties affect the overall conclusions.

6.1 CHARACTERIZING UNCERTAINTY IN QUANTIFIED EFFECTS

The data and models used to estimate costs, benefits, and other impacts inevitably involve limitations. These may relate to the quality of the methods used to collect the data, the extent to which the data address the same population, industries, or geographic area as the regulatory impacts, and the degree to which conditions may change between when the data were collected and when the regulation is implemented. In addition, the models used in the analysis, which may range from simple formulae to complex computer simulations, involve making assumptions about the relationships between various factors. All analyses require predicting how those affected will respond to the regulation, which adds to the uncertainty. The challenge for the analyst is to clearly describe (in qualitative and quantitative terms) the uncertainties related to the data, models, and assumptions in a way that aids decision-makers in understanding the confidence they should have in the results and the likely direction and magnitude of any bias.

6.1.1 BASIC CONCEPTS

Conceptually, one should distinguish uncertainty and variability. Variability refers to heterogeneity; for example, differences in the ages of those affected by a regulation. While variability can be described by statistical measures such as the standard deviation, it may be difficult to characterize precisely given that data may be

available for only a small (and perhaps non-representative) sample of those affected or for a limited geographic area or time period. The usual measure of uncertainty about a parameter when estimated from a sample of the population ("sampling variability") will be larger when there is more variability in the population (if there were no variability, even a small sample would yield an exact estimate of the parameter).[98]

In contrast, uncertainty describes lack of knowledge. For example, data on the relationship between exposure to a pathogen and the risk of mortality may be available for only a particular age group, and the agency may be uncertain whether individuals of different ages would respond similarly to the exposure. Variability is a characteristic of the real world that cannot be reduced by research (although research can lead to a better understanding of variability). In contrast, uncertainty concerns lack of knowledge and can be reduced by research.

Regulatory analysts often lack the time and resources needed to engage in substantial new primary research, and must determine how to best target their efforts. Such targeting requires using screening analysis (see Chapter 2) to identify areas where more work will have the most important implications for decision-making. Analysts must then determine how to best combine the available data with reasonable models and assumptions to characterize regulatory impacts. The limitations and uncertainties in these data, models, and assumptions must be clearly disclosed in the RIA.

The requirements in OMB *Circular A-4* (2003) encompass both variability and lack of knowledge when discussing treatment of uncertainty. OMB urges analysts to fully disclose any uncertainties inherent in the analysis and to evaluate and justify their analytical choices. OMB cautions that, at times, uncertainties may be significant enough to warrant delaying a decision until more information can be collected and assessed. This is especially true in situations where uncertainties have a significant effect on which regulatory decision appears to be best. When considering whether to recommend a delay, analysts must take into account both costs (e.g., of further data gathering efforts) and benefits (e.g., of the knowledge likely to be obtained from the new data). Delay may also have consequences for social welfare (for instance if it allows dangerous practices to continue), which must also be considered along with the impacts of any interim protective measures. If the timing of the regulation is determined by statute or court order, delay may not be possible.

6.1.2 GENERAL APPROACH

There are many options for addressing uncertainty in quantified effects. In *Circular A-4*, OMB outlines three approaches with increasing levels of complexity: qualitative discussion, numerical sensitivity analysis, and probabilistic analysis. These three methods are summarized in Table 6.1 and described in more detail below. Additional information on these approaches is provided in Morgan and Henrion (1990), Boardman et al. (2011), and other texts.

[98] Statistical or sampling variability is the variability in a statistical estimate that results when the estimate is calculated from a sample, not the full population. For example, the average height in the sample may not equal the average height in the population because a disproportionate number of tall people were sampled by chance.

TABLE 6.1. APPROACHES FOR ADDRESSING UNCERTAINTY IN QUANTIFIED EFFECTS

APPROACH	APPLICABILITY	CONDUCT
Qualitative Discussion	• For all analyses. • May suffice if: – the rule involves annual economic effects less than $1 billion; – the analyst is able to demonstrate that the results are robust to uncertainties; and, – the consequences of the rule are modest.	Disclose key assumptions and uncertainties and include information on the implications for decision-making.
Numerical Sensitivity Analysis	• For rules involving annual economic effects less than $1 billion, where: – the qualitative discussion raises questions about the robustness of the results; or, – the consequences of the rule are large.	Vary one or many parameters to calculate distinct sets of results for comparison.
Probabilistic Analysis	• For rules involving annual economic effects of $1 billion or more (required). • For rules with smaller impacts where numerical sensitivity analysis raises questions about the robustness of the results.	Develop distributions for the uncertain parameters and conduct Monte Carlo analysis to determine the distribution of the results.

Qualitative discussion of uncertainties: Qualitative discussion is the least rigorous approach, but is of significant importance. It should always be included in the RIA. This approach involves disclosing key assumptions and uncertainties and including information on the implications. To the greatest extent possible, the qualitative discussion should include both the likely direction of the potential bias (i.e., whether the assumption may lead to an under- or over-estimate of the impacts) and the likely magnitude of the effect (e.g., whether it is major or minor). Such information will help decision-makers and others better understand the implications of the analysis.

Numerical sensitivity analysis: Numerical sensitivity analysis allows the analyst to explore the effects of varying the values of key parameters and is often useful to determine whether uncertainty about particular components or assumptions may substantially affect the analytic result, as well as when data limitations or constrained resources prevent full probabilistic analysis. Sensitivity analysis can be conducted by: (1) by changing one variable or assumption at a time and calculating a new set of estimates (sometimes referred to as "partial sensitivity analysis"); or (2) by varying several variables simultaneously to learn more about the robustness of the results to widespread changes.

When conducting partial sensitivity analysis, it is generally infeasible to test all assumptions. Attention should be devoted to analyzing those assumptions or variables that are most important (in that they may have the greatest effect on the result) or are most uncertain. The analyst should vary key parameters one at a time using plausible alternative values while holding all other parameters constant. Partial sensitivity analysis can be conducted as a breakeven, or threshold, analysis; for example, where the analyst seeks to find the value of one key parameter at which quantified benefits equal costs (i.e., net benefits equal zero), as discussed later in this chapter.

Varying a combination of parameters simultaneously may obscure the effect that a single variable or assumption has on the estimates, but can be particularly useful when a group of parameters are closely related (e.g., changing demographics and participation in the labor market) or when conducting a bounding analysis. In a bounding analysis, the most- or least-favorable assumptions are selected to calculate best- or worst-case results. These two sets of results represent high-end and low-end estimates that bound the primary results of the analysis. However, care should be taken in conducting and interpreting this type of analysis, because it is

extremely unlikely that all of the parameters will simultaneously be at their highest or lowest values. Thus the outcome of an analysis that uses lower (or upper) bound estimates for all parameters is very improbable.

If the sign of the net benefits or the relative ranking of the regulatory alternatives does not change in response to sensitivity tests, analysts and decision-makers can conclude that the results are relatively robust and have greater confidence in them. Otherwise, the analyst should (1) further investigate whether it is likely that the alternative assumptions are more appropriate than the assumptions used in the original analysis; and (2) conduct more rigorous probabilistic analysis if possible.

Probabilistic analysis: Probabilistic analysis is generally most informative because it quantifies the likelihood that different results will occur. However, in some cases such analysis may not be warranted or feasible given data limitations and constrained time and resources. OMB *Circular A-4* indicates that probabilistic analysis "is appropriate for complex rules where there are large, multiple uncertainties whose analysis raises technical challenges, or where the effects cascade; it is required for rules that exceed the $1 billion annual threshold" (OMB 2003, p. 41).

Probabilistic analysis often involves the use of simulation models to quantify the probability distributions of the effects. It provides decision-makers with information about the variance, or spread, of the statistical distribution of the impacts. This information may be particularly useful when the expected value of the net benefits is close to zero or similar across multiple policy alternatives. In such cases, decision-makers may feel more confident about the results if they have a smaller variance, because the realized results are more likely to be near the expected value.

To conduct a formal probabilistic analysis, analysts must determine the joint distribution of the uncertain parameters; i.e., the distribution of each parameter together with any dependencies among them. For some parameters, such as the average body mass index (BMI) of the population when BMI has been measured for a large representative sample, the distribution can be well estimated from the sample distribution. In other cases, the probability distribution may be estimated from other data (e.g., by regression analysis), or it may be necessary to assume a distribution (e.g., uniform or triangular between upper and lower bounds) and to test whether the results are very sensitive to the assumed distribution.

Even when data are limited, distributions can be developed through formal, structured expert elicitation. Such elicitation is designed to avoid well-known heuristics and biases that can lead to poor judgment, and may be worthwhile if (1) assumptions about the distribution are likely to significantly affect the analytic results; (2) additional primary data collection is not feasible or cost-effective; and (3) sufficient time and resources are available.

Conducting structured expert elicitation requires substantial effort. Researchers first develop a well-defined question to be addressed, as well as an extensive elicitation protocol designed to ensure that the experts each interpret the questions similarly and explain the bases for their responses. Experts are identified through a formal process intended to provide a range of perspectives. The elicitation often includes supplying the experts with background materials and holding a pre-elicitation workshop to share and critique information. The elicitation is then conducted with each expert individually, frequently through a lengthy interview following a pre-determined protocol. More information on this process can be found in the expert elicitation literature (e.g., Morgan and Henrion 1990, Cooke 1991, and O'Hagan et al. 2006).

Once the joint distribution of the key parameters is estimated, Monte Carlo simulation techniques are applied to derive a probability distribution of the outcome measure, which may be total costs, total benefits, net benefits, or another impact of concern. Monte Carlo analysis involves taking a random draw from the joint distribution of the uncertain parameters (or from the distributions for each parameter if they are independent) to produce a value for each parameter; these values are then used to calculate the outcome measure. This process is

repeated many times to produce a distribution of the outcome measure, the average of which provides an estimate of its expected value.

An advantage of Monte Carlo analysis is that it provides information on the full distribution of effects, from which one can determine how likely it is that the effect exceeds any particular threshold (e.g., zero). A limitation is that the results can be sensitive to the probability distributions that are used for the input parameters, and these are often not known with much accuracy.

In sum, HHS analysts should quantify the impacts of the regulatory alternatives to the greatest extent practical.[99] The analysis should be accompanied by clear discussion of the evidence of causality as well as the quality of the studies and the statistical rigor of the methods used. However, even if the available data are of low quality or inconsistent, the impact should be quantified and accompanied by an appropriate assessment of uncertainty that clearly communicates the limitations of the analysis.[100] When time and resource constraints restrict the extent to which less significant impacts can be quantified, the evidence used to support the analytic decision should be reported. Potentially significant effects should be left unquantified only when there is no feasible approach for quantifying them.

Regardless of which approach is used to assess uncertainty, analysts should take care to avoid the appearance of false precision. Calculations should be performed without any intermediate rounding, but the results should generally be rounded for presentation in the RIA. While a variety of conventions are used in different disciplines to determine the number of significant figures to present, generally the results should be rounded to reflect the number of significant digits in the input data. For example, total costs should not be reported to the penny if the unit costs used as an input are reported in tens or hundreds of dollars.

6.2 CHARACTERIZING NONQUANTIFIED EFFECTS

Another challenge is addressing outcomes that cannot be quantified but may have important implications for decision-making. For example, available data may suggest that a regulated hazard affects the risk of both mortality and morbidity, but may not be adequate to estimate the change in some types of morbidity risks associated with each regulatory option. Without quantification, it is difficult to appropriately balance the risk reductions associated with each option against its costs, or to determine the relative importance of these different types of benefits.[101]

Quantification with appropriate treatment of uncertainty is desired (as discussed above) because it provides a clearer indication of the likely direction and magnitude of the impacts. If quantification is not possible, analysts must determine how to best provide related information. Ignoring potentially important nonquantified effects may lead to poor decisions, but there is also a danger of overemphasizing them. In the absence of information, decision-makers and others may weight nonquantified effects in a manner consistent with their own (unarticulated and perhaps unconscious) beliefs, without sufficiently probing the rationale or the weighting. Clear presentation of the available evidence is needed to counterbalance this tendency.[102]

Thus analysts should first quantify regulatory impacts to the greatest degree possible, using tools such as sensitivity and probabilistic analysis to evaluate the effects of uncertainty as discussed previously. They then should determine how to best describe those effects that remain unquantifiable, to provide insights into their significance in comparison to each other and to the quantified impacts, as discussed below.

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[99] OMB *Circular A-4* states: "[t]o the extent feasible, you should quantify all potential incremental benefits and costs" (OMB 2003, p. 45).

[100] Determining how to best apply the available research requires careful review of the evidence and substantial professional judgment. A number of approaches, such as criteria-driven systematic review, meta-analysis, and structured expert elicitation, can be used to develop estimates in cases where the research varies in quality and provides inconsistent results. The benefit transfer framework, discussed in Chapter 3, also can be applied to other types of quantities to develop estimates from data on somewhat dissimilar effects.

[101] We use the term "quantification" to refer to the consequences of the regulation (generally measured in physical units, such as cases averted), and monetization to refer to the dollar value of those consequences.

[102] OMB *Circular A-4* (2003) indicates that nonquantified effects should be included in the summary table discussed in Chapter 8.

6.2.1 BASIC CONCEPTS

Analysts may be unable to estimate some potentially important regulatory impacts due to gaps in the available data, the nature of the impacts themselves, or the need to focus on assessing more significant effects due to time and resource constraints. For example, analysts may not have the data needed to estimate the effect of the regulation on disease incidence, even though the available research suggests that the disease is associated with the regulated hazard. In the case of costs, analysts may have evidence that the regulation will lead to significant innovation, but may not be able to predict or describe the likely innovations adequately to estimate the impacts in monetary terms.

Another example is information provision. Some regulations increase the type or quality of information available and its dissemination, but research may be lacking on how recipients are likely to respond. Thus while an intermediate measure may be available, such as the number of patients who receive information on potentially beneficial lifestyle changes, it may not be possible to translate this measure into a quantity that can be monetized to estimate benefits. The latter requires an estimate of the change in behavior that results and of how the behavioral change affects individual welfare; e.g., of the degree to which the risk of illness or death is reduced. While these types of deficiencies ideally would be remedied through additional primary research, such research may require more time and resources than immediately available. HHS agencies should, however, try to anticipate future analytic needs and invest in research that will be useful across several regulatory analyses.

In other cases, the lack of quantification may result because the effects are less tangible and more subject to normative judgment. They may involve important human values, such as dignity, equity, and privacy. While it may be difficult to quantify the change in these values attributable to a particular regulation, it may be possible to count the number of people affected or report other intermediate measures.

Any intermediate measures, such as these counts, should be presented in the analysis as indicators of potential costs or benefits. For example, if analysts have information on the number of organizations subject to a regulatory provision, but lack the information needed to estimate related costs, or they have information on the number of individuals affected, but lack the data needed to estimate a particular benefit, these counts should be reported. Such intermediate measures should also be reported when the resulting benefits and costs are fully quantified, to promote better understanding of the analytic results.

6.2.2 GENERAL APPROACH

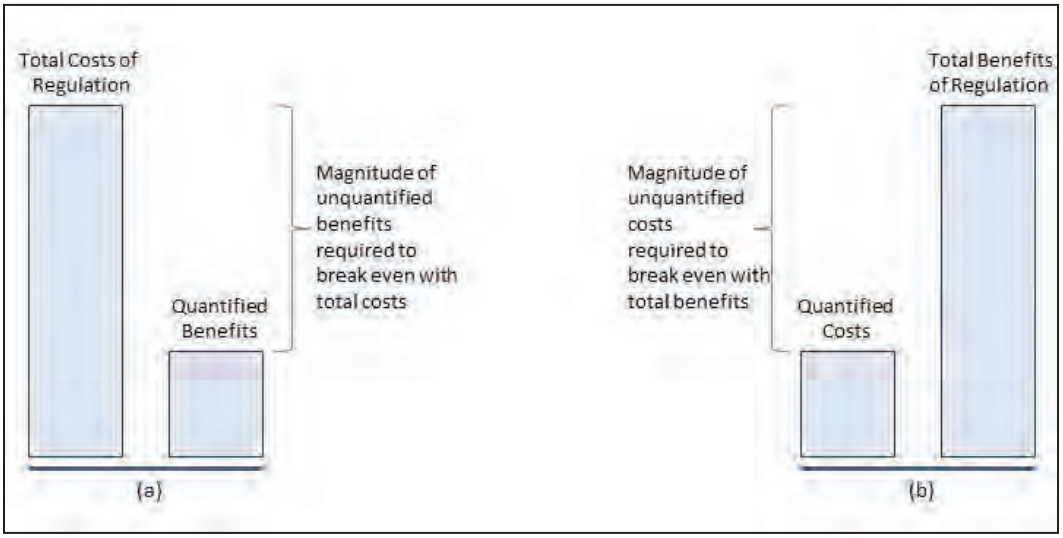
Options for incorporating nonquantified effects into the regulatory analysis depend on the available data and include both quantitative and qualitative approaches. Approaches that involve some calculation (and may be particularly useful when comparing benefits and costs) include breakeven, cost-effectiveness, and bounding analysis, but care must be taken to avoid misinterpretation of the results. More qualitative approaches include the use of tables and graphics as well as text discussions.

HOW SHOULD NONQUANTIFIABLE EFFECTS BE ADDRESSED?

If it is not possible to quantify an impact, analysts should consider using breakeven, cost-effectiveness, or bounding analysis, as well as tables and text, to illustrate the potential implications.

Breakeven analysis: Breakeven analysis, sometimes referred to as threshold analysis, asks the question "how large would the nonquantified effect(s) have to be, to bridge the gap between quantified benefits and costs?" Figure 6.1 provides an example of this concept. Part (a) shows the case where only some of the benefits can be quantified; part (b) illustrates the case where only some of the costs can be quantified.

FIGURE 6.1. BREAKEVEN ANALYSIS



Generally, breakeven analysis can only be conducted for a single quantity. Thus breakeven analysis is useful when analysts are particularly uncertain about one key parameter. For example, analysts may have information on the value of the effect (e.g., the VSL in the case of mortality risk reductions) but not the physical effects (e.g., the number of statistical cases averted). In this case, the breakeven analysis would be used to estimate the number of averted cases needed for benefits to exceed costs, given the VSL. Similarly, for costs, it may be possible to estimate the number of firms affected by a particular provision, but not the cost per firm. Breakeven analysis can be used to provide insight into how large the cost per firm would need to be for the costs to exceed the benefits of that provision. It can also be used to identify the breakeven probability of occurrence that would equalize costs and benefits.

Once the analysis is conducted, decision-makers and stakeholders can inspect the results to judge whether it is likely that the nonquantified effects are large enough to fill the gap. Breakeven analysis is most useful when some information is available on the potential magnitude of the impact, to provide a basis for judging whether the nonquantified effects can plausibly exceed the breakeven amount. It also may be informative when data are available but not public. For example, confidential information on the likelihood and consequences of terrorist attacks may be available to decision-makers but not to regulatory analysts or the general public. This information could provide context for decision-makers' review of the breakeven results for a regulation that addresses homeland security.

Cost-effectiveness analysis: Cost-effectiveness analysis is another approach that can provide insights when an impact can be quantified but cannot be assigned a monetary value (see Institute of Medicine 2006, Drummond et al. 2015). Under this approach, a monetary estimate of the costs (net of any monetized benefits) is divided by an effects measure to determine the cost per unit of effect. The effect could be the number of deaths averted, QALYs gained (see Chapter 3 and Appendix C), individuals treated, or another measure. Care must be taken, however, in interpreting the results. Cost-effectiveness ratios do not indicate whether an intervention is worth undertaking (i.e., whether the value of the benefits exceeds the costs), nor which option is likely to yield the largest net benefits.

Bounding or "what-if" analysis: Bounding analysis considers the extent to which benefits are likely to exceed costs based on lower- or upper-bound estimates of the magnitude of the nonquantified effects. For example, if the available data are sufficient to estimate that the mortality risk reductions associated with the regulation are unlikely to be greater than 1,000 statistical cases or fewer than 10 statistical cases, then the results could be presented using both estimates. "What if" analysis is similar, and involves investigating the impact of various hypothetical, but plausible, scenarios on the results. For example, the analyst could compare benefits and costs

for mortality risk reductions ranging from 10 to 1,000 statistical cases, if he or she believes that outcomes within this range are possible, and report the extent to which benefits exceed costs under each scenario.

The dividing line between these approaches and standard sensitivity analysis (discussed above) is somewhat vague. In concept, bounding or "what-if" analysis in this case would involve very wide ranges based on relatively little data or supporting evidence, and would be presented separately from the primary estimates of benefits and costs due to the high degree of speculation involved.

Tables and graphics: Tables and graphics are often useful for highlighting nonquantified effects, to ensure that they are not overlooked by decision-makers and others. One option is to simply list the effects in a table; however, the list is likely to be more useful if the effects can be categorized in a way that indicates the implications for decision-making. This categorization could include whether the effects are likely to be large or small, and to lead to over- or underestimates. Separate categories or exhibits could be used to report the strength of the evidence that links the effect to the regulation, the likelihood of its occurrence (e.g., high or low), or the extent to which it is reversible, as well as other attributes that will be salient for decision-making.

Table 6.2 below provides an example that uses symbols to highlight the potential magnitude of the impacts.[103] Alternatively or in addition, analysts could insert text into the table to provide more information than can be conveyed by a symbol. Such tables can also be used to separately indicate the effects on benefits and costs, rather than solely focusing on net benefits as in the example.

TABLE 6.2. EXAMPLE OF SUMMARY OF NONQUANTIFIED EFFECTS

EFFECT OF NONQUANTIFIED IMPACTS ON NET BENEFITS	POTENTIAL MAGNITUDE*
Analysis may overstate net benefits	
• impact "a"	
• impact "b"	
• etc.	
Analysis may understate net benefits	
• impact "c"	
• impact "d"	
• etc.	
Analysis may under- or overstate net benefits	
• impact "e"	
• impact "f"	
• etc.	

*Dashed vertical line indicates quantified net benefits.

Text discussion: All of the approaches described above must be accompanied by text that clearly defines the nonquantified effects, explores the causal evidence that links them to the regulatory action, summarizes available information on their direction and magnitude, and discusses the conduct and interpretation of related analysis, including both the results and related uncertainties.

[103] Microsoft Excel and similar programs allow the user to represent quantities graphically; for example, to automatically size an arrow that represents the quantity "10" so that it is twice the size of an arrow that represents the quantity "5." While such features may be useful when analysts have some information on relative magnitudes, care should be taken to not mislead readers about the extent to which the size of the symbols represents evidence on the expected size of the effect.

In sum, the treatment of nonquantified impacts should be tailored to the characteristics of the effect (such as whether it involves intangibles or normative values), the extent to which relevant data are available, and the importance of the effect for decision-making. These impacts should be clearly defined and distinguished from the quantified impacts, to avoid the potential for double-counting.

At minimum, analysts should list significant nonquantified effects in a table and discuss them qualitatively. To the extent possible, the effects should be categorized or ranked in terms of their importance and implications for choosing among the regulatory alternatives (including the option of no action). Where some data exist, but are not sufficient to reasonably quantify the effect, analysts should consider whether breakeven, cost-effectiveness, or bounding analysis will provide useful insights. Intermediate measures, such as the number of individuals affected, should be reported where available. Where impacts can be monetized but not quantified, the monetary value per unit of impact (e.g., the value per averted statistical case in the case of health impacts) should be reported.

Chapter 7

Conduct Distributional and Other Supplementary Analyses

The previous chapters focus largely on the benefit-cost analysis that is the core of the RIA. However, agencies must also comply with a number of other analytic requirements. These include considering the distribution of benefits and costs across demographic or other population subgroups as well as complying with several other executive orders and statutes. In addition, for those regulations with impacts outside of the U.S., analysis of international impacts is required. These analyses should be reported in clearly labeled, separate sections of the regulatory analysis (see Chapter 8), which discuss the available evidence and related uncertainties as well as the implications for decision-making.

7.1 ASSESS DISTRIBUTION ACROSS DEMOGRAPHIC GROUPS

In addition to estimating the national net benefits of the policy options, HHS and other regulatory agencies are required to separately address how the benefits and costs of their economically significant regulations are distributed. The benefit-cost analysis discussed previously focuses on the net impact of the regulation on social welfare, while the distributional analysis focuses on the incidence of the benefits and costs.

In this section, we discuss the distribution of impacts across individuals with differing demographic or other characteristics. Such analysis is encouraged under Executive Orders 12866 and 13563 (Clinton 1993, Obama 2011), as well as by OMB *Circular A-4* (2003), and includes analyses required by Executive Order 13045, “Protection of Children from Environmental Health Risks and Safety Risks” (Clinton 1997), and Executive Order 12898, “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations” (Clinton 1994), where applicable.[104]

This analysis is intended to provide descriptive information for consideration by decision-makers and stakeholders; it should not assign values to reflect distributional preferences or make normative judgments related to the fairness or equity of the impacts. In many cases this analysis will be primarily qualitative or rely largely on simple screening; in those cases where distributional concerns are more significant, it will be more extensive and detailed.

7.1.1 BASIC CONCEPTS

The goal of distributional analysis is to provide information on how benefits and costs affect different groups, so as to make trade-offs between economic efficiency and distributional concerns more explicit. Decision-makers may choose the economically-efficient regulatory option that maximizes net benefits, or may choose a less efficient option to ameliorate distributional impacts or achieve other policy goals.

Generally, the distribution of both benefits and costs should be considered, so that decision-makers and others can consider the extent to which the impacts are counterbalancing for each group as well as the overall distribution of net benefits across groups. In addition to understanding the incremental effects of the regulation, analysts may wish to provide information on the distribution under the “without new regulation” baseline as well as on the distribution that results under each policy alternative.

The starting point for distributional analysis is the national assessment of social benefits and costs, discussed in Chapters 3 and 4. However, as noted in Chapter 4, transfer payments are generally not included in the benefit-cost analysis, but must be considered in the distributional analysis.

[104] See the National Archives website for a complete set of executive orders (http://www.archives.gov/federal-register/executive-orders/disposition.html).

A key step in the analysis involves identifying which population groups should be considered.[105] In some cases, groups of concern may be defined by statute. In addition, Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations" (Clinton 1994), requires agencies to identify and address "disproportionately high and adverse human health or environmental effects" on these groups. Executive Order 13045, "Protection of Children from Environmental Health Risks and Safety Risks" (Clinton 1997), requires agencies to identify and address risks that may disproportionately affect children. Other groups of concern may emerge in the course of the analysis. For example, analysts may find that the effects of the regulations are likely to be concentrated in certain geographic areas or among groups with particular characteristics, such as the homeless, the HIV-infected, or those with specific dietary habits.

It is often tempting to focus solely on adverse effects on disadvantaged groups. However, such focus is problematic because it leads analysts to ignore potential beneficial effects that may be of equal or greater importance. Any distributional effect involves both "from" and "to" sides of the equation; who gains may be as important as who loses. The benefits and costs of the regulation may be counterbalancing, or may differentially affect the advantaged and the disadvantaged.

When describing these effects, one option is to provide a table or graph that reports the percentage and value of the costs, benefits, and net benefits that accrue to individuals or households at different points in the distribution; e.g., to income quintiles. Other measures for describing inequality are available; their advantages and disadvantages are discussed in detail in several sources.[106]

7.1.2 GENERAL APPROACH

Assessing the distribution of regulatory benefits and costs, as well as net benefits, can be challenging. As noted earlier, the conduct of such analysis is likely to vary significantly depending on the nature of the regulation, the characteristics of its benefits and costs, the population groups of interest, and the data and other analytic resources available. Screening analysis (see Chapter 2) can be useful in determining how to best focus this effort. Below, we discuss some of the challenges related to assessing the distribution of regulatory costs and health-related benefits, which affect analysts' ability to address each independently as well as their net effect.

WHAT ARE THE REQUIREMENTS FOR DISTRIBUTIONAL ANALYSIS?

At minimum, analysts should include a short description of the likely distribution of benefits and costs across individuals or households in different population groups, including low income and minority groups and children as discussed in Executive Orders 12898 and 13045. Requirements for other types of distributional analysis are discussed in the next section.

Distribution of regulatory costs: In the case of regulatory costs (and off-setting savings), we are typically interested in the monetary expenditures needed to comply with the regulatory requirements (including transfers), measured in dollar terms, and the ultimate effect on the disposable income of the groups of concern. Where regulatory costs are borne directly by individuals and households, the main challenge is determining how the costs are distributed across those who belong to different groups, which may be identified, for example, by income quintile, minority status, or degree of health impairment.[107] Where the costs are borne initially by firms, assessing the effects on individuals and households in different groups requires additional steps.[108] We first need to know how regulatory costs imposed on these entities translate into changes in unit prices paid by

[105] OMB *Circular A-4* (2003) defines distributional effects broadly as including, for example, how regulatory impacts are divided across "income groups, race, sex, industrial sector, geography" as well as over time.

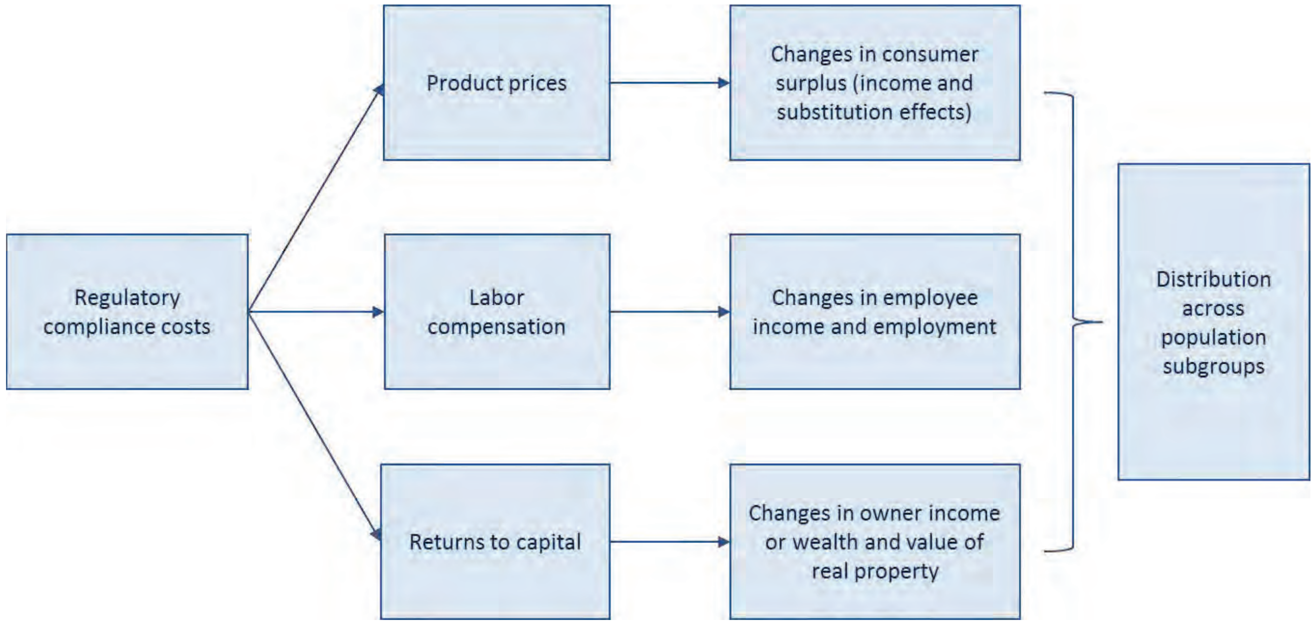
[106] For a general overview of options for addressing distributional concerns in policy analysis, see Weimer and Vining (2011), Chapter 7. For further discussion, see Boardman et al. (2011).

[107] Consumer behavior will also affect the distribution of these costs. For example, if the price of a food is increased, some may substitute an alternative food. This substitution may affect both the costs and the benefits incurred, and such behavioral responses may vary across population groups.

[108] If the organizations are not-for-profit, similar principles apply although the nature of the impacts may differ. If the costs are initially incurred by a government unit, then the analysis would address how that unit is funded; i.e., the distribution of taxes, users fees, or other revenue sources.

consumers (including both income and substitution effects), in wages paid to employees, and in returns to capital that accrue to owners, as illustrated in Figure 7.1.

FIGURE 7.1. DISTRIBUTION OF INDUSTRY COSTS ACROSS INDIVIDUALS AND HOUSEHOLDS



As in the benefit-cost analysis, the distributional analysis must clearly differentiate the impacts of the new policy from the impacts of other factors that should be reflected in the "no new regulation" baseline projections. At times, retrospective analysis may be available that addresses similar regulations and uses statistical tools to distinguish the effects of regulatory costs.[109] Interviews with members of the affected industry may also be useful. Otherwise, the extent to which each of the pathways in Figure 7.1 can be assessed will depend largely on the data available from the benefit-cost analysis. If only direct compliance costs are estimated, then it may be difficult to estimate how the costs are allocated across consumers and producers. If partial equilibrium modeling is included (which estimates changes in consumer and producer surplus), more sophisticated distributional analysis is possible. In a few cases, where regulations are expected to have significant impacts throughout the economy, results for model households from general equilibrium modeling may also be available. In all cases, the analysis of total social costs will exclude transfers, which will need to be estimated to assess the distribution of the impacts.

The allocation of costs across producers and consumers will also depend on the timeframe considered. Some costs that are fixed in the short run will be variable in the long run. For example, in the near term firms may not be able to make major changes in their physical plant (and some may close due to the costs of complying with the regulation), but such changes become more possible in the future, affecting how the costs are distributed.

Distribution of health benefits: In the case of benefits, some regulations may primarily provide savings in monetary costs, in which case the distributional analysis would proceed along the same lines as described above although the effects are likely to be in the opposite direction – savings potentially decrease prices, increase wages, and increase returns to capital. When the benefits involve reduced mortality and morbidity risks, there are several options for measuring the effects on each group. We can count the number of statistical cases averted (by multiplying the expected individual risk reduction by the number of people affected); we can use integrated measures (such as quality-adjusted life years, QALYs) to estimate the net effect on health-related

[109] For employment impacts, see Morgenstern (2013) for a comprehensive review.

quality of life and longevity; and we can use monetary measures that indicate the amount those affected would be willing to pay for the risk reductions (see Chapter 3).

In general, the distribution of health effect incidence is easier to calculate than the distribution of costs. The benefit analysis is likely to provide estimates of the number of people affected; the challenge is then to identify how the effects are allocated across the groups of concern.[110] In some cases, the characteristics of the regulation may aid in estimating this distribution. For example, if a food safety regulation affects the risks associated with drinking juice, and the distribution of juice drinking across groups (categorized by income, age, or other demographic attributes) is known, the analysis may be relatively straightforward. The risk assessment that supports the regulation will often provide related information. It typically summarizes or references available data on populations that may be particularly sensitive or vulnerable to the effects of the regulated hazard, including those who may be disproportionately affected due to health conditions, age, or socioeconomic status. In addition, HHS maintains several population databases that provide information on the characteristics of those who experience various types of health effects. Examples include the National Health Interview Survey and the Medical Expenditure Panel Survey.

In sum, the discussion above suggests that distributional analysis may be quite complex, and requires thinking carefully about what types of information will be most useful to decision-makers given the characteristics of the regulation and of those it is likely to affect. In some cases, the analysis may be primarily qualitative; in others more detailed quantitative assessment will be warranted. Analysts should follow a phased approach to ensure that the assessment is well-focused and useful for decision-making, using screening analysis as discussed in Chapter 2. Both gains and losses among advantaged and disadvantaged groups should be considered, to ensure that any counterbalancing or exacerbating impacts are taken into account.

7.2 CONDUCT SUPPLEMENTARY ANALYSES

Several other types of analysis are required by various statutes and executive orders. In general, all of these requirements should be addressed; however, the extent to which detailed analysis is required will depend on the characteristics of the specific rule. Table 7.1 summarizes these requirements and directs the analyst to additional guidance documents. The basic requirements are discussed in more detail below.

[110] As noted earlier, to the extent that people may alter their behavior in response to the regulation (e.g., taking less precaution in handling food when packaging is improved), any difference in this response can affect the distribution of benefits.

TABLE 7.1. REQUIREMENTS FOR SUPPLEMENTARY ANALYSES

REQUIREMENT	APPLICABILITY	GUIDANCE DOCUMENTS
Regulatory Flexibility Act: Requires agencies to consider the impact of regulatory actions on small entities, analyze effective alternatives that minimize small entity impacts, and make their analyses available for public comment.	All regulations subject to notice and comment under section 553(b) of the Administrative Procedures Act. Note: a full regulatory flexibility analysis is not required if the agency can certify that the proposed rule will not "have a significant economic impact on a substantial number of small entities" (5 U.S.C. §605(b)). HHS provides guidance defining a "substantial number" and "significant effect" (see HHS 2003).	• *A Guide for Government Agencies: How to Comply with the Regulatory Flexibility Act* (SBA 2012) • *Guidance on Proper Consideration of Small Entities in Rulemakings of the U.S. Department of Health and Human Services* (HHS 2003)
Unfunded Mandates Reform Act: Requires agencies to assess the effects of regulatory actions on State, local, and tribal governments, and the private sector.	All "significant" rulemakings – defined as those likely to result in the expenditure by State, local, or tribal governments, in the aggregate, or by the private sector, of $100 million or more in any one year in 1995 dollars, adjusted for inflation.	• "Guidance for Implementing Title II of S.1" (OMB 1995) • Annual memorandum from HHS updating "significant rulemaking" threshold value (e.g., HHS 2014)
Executive Order 13132 ("Federalism"): Requires agencies to develop a process to ensure meaningful and timely input by State and local officials.	All policies that have "substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government."	None.
Paperwork Reduction Act: Requires agencies to estimate the information collection (reporting, recordkeeping, and third-party disclosure) burden associated with their actions.	All policies that require generation, maintenance, or provision of information to or for a Federal agency. Agencies must obtain approval from OMB prior to requesting the same information from 10 or more individuals.	• Paperwork Reduction Act Primer (Sunstein 2010b) • OMB's website Federal Collection of Information • HHS's website Frequently Asked Questions about PRA/Information Collection • Agency's designated PRA team

7.2.1 REGULATORY FLEXIBILITY ACT

The Regulatory Flexibility Act of 1980 (RFA), as amended by the Small Business Regulatory Enforcement Fairness Act (SBREFA) (5 U.S.C. 601, *et seq.*), "requires agencies to consider the impact of their regulatory proposals on small entities, analyze effective alternatives that minimize small entity impacts, and make their analyses available for public comment" (SBA 2012). Small entities include small businesses, not-for-profit organizations, and governmental jurisdictions, definitions of which can be found within Section 601 of the RFA. In addition, the U.S. Small Business Administration (SBA) has developed size standards to define small businesses, which can be found in 13 CFR 121.201. The RFA requirements have been extended to small rural hospitals through Section 1102(b) of the Social Security Act (42 U.S.C. §1302). Definitions of "small," "rural," and "hospital" are provided in the Medicare regulations at 42 CFR 412.

If a proposed rule is not expected to have a significant impact on a substantial number of small entities, the agency may certify that this is the case, and must provide a statement providing the factual basis for this determination. If the agency cannot provide this certification, or is uncertain about the rule's impact, it should prepare an Initial Regulatory Flexibility Analysis (IRFA) for publication with the proposed rule. Section 603 of the RFA lists the information that must be included in the IRFA.

For the final rule, if the agency cannot provide this certification or remains uncertain after reviewing public comment on the proposed rule, a Final Regulatory Flexibility Analysis (FRFA) should be prepared and published. The requirements for the FRFA are similar to those for the IRFA and are outlined in Section 604 of the RFA. When it prepares a FRFA, the agency must also publish one or more small entity compliance guides to inform small entities of their obligations and responsibilities under the rule.

Detailed guidance on compliance with the RFA and preparation of the regulatory flexibility analysis can be found in the SBA's *A Guide for Government Agencies: How to Comply with the Regulatory Flexibility Act* (SBA 2012).[111] This document walks agencies through the process of preparing screening analyses and initial and final regulatory flexibility analyses. In addition, HHS's *Guidance on Proper Consideration of Small Entities in Rulemakings of the U.S. Department of Health and Human Services* (HHS 2003) supplements the SBA guidance, providing examples of issues that commonly arise in applying the RFA and SBREFA to HHS rulemakings.

7.2.2 UNFUNDED MANDATES REFORM ACT

The Unfunded Mandates Reform Act (UMRA) (2 U.S.C. §1501 *et seq.*) seeks to curb the practice of imposing unfunded Federal mandates on State and local governments. UMRA Section 1531 requires Federal agencies to assess the effects of their regulatory actions on State, local, and tribal governments, and the private sector. Section 1532 requires them to prepare a written statement that assesses the costs, benefits, and other effects of proposed or final rules for significant regulatory actions (2 U.S.C. §1532(a)). UMRA defines significant regulatory actions as those that include a Federal mandate likely to result in the expenditure by State, local, or tribal governments, in the aggregate, or by the private sector, of $100 million or more in any one year (in 1995 dollars) (2 U.S.C. §1532(a)). This threshold is adjusted each year for inflation.

Most of UMRA's requirements are fulfilled by the RIA that is prepared to comply with Executive Orders 12866 and 13563 (Clinton 1993, Obama 2011) and OMB *Circular A-4* (2003), as discussed in the earlier chapters of this guidance. Additional guidance on the preparation of written statements under UMRA can be found in OMB's 1995 "Guidance for Implementing Title II of S.1." In addition, HHS releases an annual memorandum updating the threshold value (adjusted for inflation) for a significant regulatory action (see, for example, HHS 2015).[112]

7.2.3 FEDERALISM

Executive Order 13132, "Federalism" (Clinton 1999), emphasizes consultations with State governments and enhanced sensitivity to their concerns in cases where regulatory or other policy actions impinge on their constitutionally established role as sovereign entities. It requires Federal agencies to develop an accountable process to ensure "meaningful and timely input by state and local officials in the development of regulatory policies that have federalism implications." Section 1(a) defines policies that have federalism implications to include regulations that have "substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government."

Under Executive Order 13132, Federal agencies may not issue a regulation with Federalism implications that imposes substantial direct compliance costs and that is not required by statute unless the Federal government provides the funds necessary to pay the direct compliance costs incurred by State and local governments or the agency consults with State and local governments in the process of developing the proposed regulation. The agency also may not issue a regulation with Federalism implications that preempts a State law without consulting with State and local officials.

[111] This and other material related to implementation of the RFA is available on the Regulatory Flexibility Act (http://www.sba.gov/category/advocacy-navigation-structure/regulatory-flexibility-act) page of the SBA website.
[112] The method and sources used to update this threshold value are described in HHS (2015).

7.2.4 PAPERWORK REDUCTION ACT

The Paperwork Reduction Act (PRA) (44 U.S.C. §3501 *et seq.*) requires Federal agencies to estimate the information collection burden associated with all of their actions. The term "burden" means the time, effort, or financial resources expended by persons to generate, maintain, or provide information to or for a Federal agency. Agencies must obtain approval from OMB prior to requesting the same information from ten or more individuals. Thus, if a proposed regulation will impose such a burden (e.g., a regulation may require regular reporting of compliance data to HHS), the agency must prepare an information collection request (ICR) for review and approval by OMB.

Paperwork burdens or costs are a subset of the total costs of a regulation and should be included in those costs (see Chapter 4).[113] The paperwork burden of a regulation includes the incremental cost of required record keeping, reporting, and public disclosure. It includes only the incremental data collected as a result of the regulation; data collections required by the rule that are already undertaken for other purposes are considered part of the baseline and are not part of the collection burden under the PRA. For example, a rule requiring facilities to maintain records on health and safety-related maintenance practices may not result in an incremental collection burden if these records are already collected by the facility for other purposes, such as payroll. As with estimates of other compliance costs (see Chapter 4), it is important to isolate the incremental burden of the regulation when preparing the ICR.

7.3 ADDRESS INTERNATIONAL EFFECTS

The regulatory analysis should generally focus on benefits and costs that accrue to U.S. citizens and residents. However, regulations that address trade barriers and other market failures may have an effect on both the United States and its trading partners. In cases where regulations have impacts outside of the United States, they should be addressed in a supplementary analysis. Following the guidance in OMB *Circular A-4* (2003), these international effects should be reported separately from those occurring within the U.S.[114]

International effects may include direct economic impacts (e.g., related to increases or decreases in international trade) as well as any other potentially significant effects. For example, increasing safety requirements for U.S.-based food manufacturing may provide health benefits to countries that import this food; decreasing the transmission of disease in the U.S. is likely to decrease the risk of transmission to residents of other countries.

In general, analysis of international effects should include impacts on imports and exports. Partial equilibrium analysis using publicly available information on import supply and demand elasticities can be used to model how a regulation might change the flow of imports and exports. More complicated general equilibrium analysis may be required if an entire sector of the economy is affected. For additional information on these types of modeling, see Chapter 4.

The analysis of international effects may also include impacts on foreign entities whose U.S. operations are affected. It is often difficult to identify U.S. subsidiaries of foreign entities and report impacts to their operations separately from those to U.S.-based businesses. Therefore, impacts on U.S. subsidiaries are often included in the main analysis. If this is the case, and the analyst thinks that impacts on U.S. subsidiaries of foreign entities may be substantial, the analysis should include a qualitative discussion of the effect.

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[113] There are important differences in the requirements of the PRA and the best practices for preparing RIAs as discussed in the prior chapters. For a detailed discussion of the PRA requirements, see the sources referenced in Table 7.1.

[114] Executive Order 13069 (Obama 2012) includes requirements for identifying regulations that may have significant international impacts.

For more information on how to address international effects, see OMB's *2008 Report to Congress on the Benefits and Costs of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities* (OMB 2008) and the *Review of the Application of EU and US Regulatory Impact Assessment Guidelines on the Analysis of Impacts on International Trade and Investment* (OMB and the Secretariat General of the European Commission 2008).[115]

[115] OMB's reports to Congress are available on the OIRA Reports to Congress (http://www.whitehouse.gov/omb/inforeg_regpol_reports_congress/) page of its website.

Chapter 8

Communicate the Approach and Results

Regulatory analyses must be clearly and comprehensively documented in an RIA, which may be published in full in the preamble to the *Federal Register* notice for the proposed or final rule, or as a separate report, in which case it must be summarized in the preamble. The RIA must describe the rationale for the regulation, the options considered, the analytic approach, and the results, as well as the implications of uncertainties. For regulations with particularly large or complex impacts, it may be necessary to provide additional information in technical reports that supplement the main analysis.

Without clear communication, the RIA will not meet its intended goal of informing related decisions. This communication should address two audiences. First, it should be written so that members of the lay public can understand the analysis and conclusions. Second, it should provide enough detail so that competent analysts could ideally reconstruct the analysis, or at minimum explore the implications of changing key assumptions. This chapter briefly describes related practices.

8.1 DESCRIBE THE ANALYSIS AND RESULTS

The audience for the RIA is diverse and includes many who lack the technical expertise and knowledge of those who conducted the analysis. Given that the purpose of the analysis is to inform decision-makers and other stakeholders, it is critical that it be described in terms that can be easily understood by a lay audience. At the same time, the documentation must be sufficient to support future work, including replication, testing the effects of alternative assumptions, applying the same or similar approaches in a future analysis, or reconstructing the analysis as part of a retrospective assessment.

The main text should provide a succinct and clear summary of the analysis. Technical details should be provided in appendices or supporting documents. The main text may, for example, include the following major sections, reflecting the requirements in OMB *Circular A-4* (2003) as well as the requirements provided in this guidance document. Those sections that provide analytic results should also include a subsection that discusses the implications of uncertainties, as described in Chapter 6.

1) Executive Summary (see additional discussion below)
2) Statement of the need for the regulation
3) Characterization of the without-regulation baseline
4) Description of the regulatory alternatives (including the preferred alternative)[116]
5) Benefits of the regulatory alternatives
6) Costs of the regulatory alternatives
7) Comparison of benefits and costs
8) Supplementary analyses
    a) Distribution of benefits and costs
    b) Regulatory Flexibility Act analysis
    c) Unfunded Mandates Reform Act analysis
    d) Other analyses
    e) International effects

[116] These alternatives may include both regulatory and non-regulatory approaches, as described in Chapter 2.

In particular, the executive summary must use plain English and be designed to promote public understanding. OMB (2012) suggests that executive summaries include a statement of need for the regulation; a summary of the major provisions of the regulatory action; and, for economically significant rulemakings, a table summarizing the benefits and costs. For additional guidance on the format for Executive Summaries see "Clarifying Regulatory Requirements: Executive Summaries" (OMB 2012).

8.2 PROVIDE SUMMARY TABLES AND FIGURES

The RIA should include tables and figures that clearly convey the results of the analysis.

Key information to be summarized includes:

- Annual benefits and costs (undiscounted);
- Annualized and present value costs;
- Annualized and present value benefits;
- Net benefits (i.e., benefits minus costs) presented on an annualized basis and, as appropriate, in present value terms.

These quantified results should be accompanied by information on important nonquantified impacts.

In addition to "central" or "best" estimates, information on uncertainty must also be presented. When reporting annualized or present value impacts, analysts must indicate the time period over which impacts are estimated.[117] Results should be presented for discount rates of both three and seven percent.

Depending on the complexity of the analysis and the number of cost and benefit categories, the results may be summarized in a single or multiple tables or figures. Each should reference the information sources and note key assumptions. While such exhibits are essential to focus attention on key findings, analysts should keep in mind that some readers will skip over the more detailed technical information in the text. Thus clear labeling is needed to ensure that the contents of the tables and figures are not misinterpreted. Additionally, the associated text should interpret each table or figure for the reader. It may improve communication to supplement the results tables with charts and graphs that summarize and highlight key steps in the analysis as well as the major conclusions and their implications.

For economically significant rules, agencies are also required to provide OMB with an accounting statement that includes a standard table reporting benefit and cost estimates. Figure 8.1 provides a suggested format for this accounting statement, adapted from OMB *Circular A-4*. The accounting statement summarizes the information presented in the RIA and should include:

- Annualized incremental benefit and cost estimates, using real discount rates of three and seven percent, within the following three categories: monetized; quantified, but not monetized; and qualitative, but not quantified or monetized. The primary benefit and cost estimates should reflect the expected values. The minimum and maximum estimates should, if possible, reflect the 5th and 95th percent confidence bounds.
- Annualized incremental transfer estimates, which occur when wealth or income is redistributed without any direct change in aggregate social welfare.
- Information on the effects on State, local, and tribal governments, small businesses, wages, and economic growth.

[117] As discussed in Chapter 2, for meaningful comparison, benefits and costs should be measured over the same time period. When some impacts are assessed over longer periods than others to provide important information for decision-making, the results for the additional period should be reported separately to avoid misleading comparisons.

FIGURE 8.1. TEMPLATE FOR OMB ACCOUNTING STATEMENT

OMB #: **Agency/Program Office:**
Rule Title:
RIN#: **Date:**

Economic Data: Costs and Benefits Statement							
				Units			
Category	Primary Estimate	Low Estimate	High Estimate	Year Dollars	Discount Rate	Period Covered	Notes
Benefits							
Annualized Monetized $ millions/year					7%		
					3%		
Annualized Quantified					7%		
					3%		
Qualitative							
Costs							
Annualized Monetized $ millions/year					7%		
					3%		
Annualized Quantified					7%		
					3%		
Qualitative							
Transfers							
Federal Annualized Monetized $ millions/year					7%		
					3%		
From/To	From:			To:			
Other Annualized Monetized $ millions/year					7%		
					3%		
From/To	From:			To:			
Effects							
State, Local or Tribal Government:							
Small Business:							
Wages:							
Growth:							

In addition to the present value and annualized results, OMB *Circular A-4* suggests that the analyst include separate schedules of undiscounted monetized benefits and costs showing the type and timing of these effects, as discussed in Chapter 5. These undiscounted results should be presented in constant dollars for each year of the analytic time horizon. Again, this schedule could be presented in a table or as a bar chart or other graphic.

In sum, presenting the analysis so that it can be easily understood by decision-makers and stakeholders may require significant effort to clearly and concisely describe the options assessed, the analytic approach, and the results. Without such effort, the analysis may not play its intended role in the decision-making process, and may be misconstrued in ways that lead to significant and unnecessary controversy. Avoiding technical jargon, and using tables and graphics to illustrate key points, will aid in ensuring that the analysis is useful for decision-making.

Chapter 9

Conduct Retrospective Analysis

Executive Order 13563 directs each Federal agency to establish a plan for ongoing retrospective review of existing significant regulations to identify those that can be eliminated as obsolete, unnecessary, burdensome, or counterproductive, or that can be modified to be more effective, efficient, flexible, and streamlined (Obama 2011, HHS 2011).[118] The initial HHS plan was finalized in August 2011 and has been subsequently updated.[119]

The plan describes HHS's approach for identifying regulations for review as part of an ongoing process and lists factors HHS routinely considers in this review (HHS 2011). The factors include many that can be evaluated qualitatively; for example, identifying redundant or obsolete regulations or requirements. While important for a broader program of retrospective review, such qualitative analysis is not the focus of this guidance. Rather, this chapter describes HHS's approach for quantitative retrospective analysis of the benefits and costs of selected economically significant regulations.

Quantitative retrospective benefit-cost analysis may serve several purposes, ranging from assessing the effectiveness of a single regulation to evaluating the overall use of benefit-cost analysis in the regulatory development process. The next section discusses the conceptual framework in greater detail. We follow with an overview of the approach to retrospective benefit-cost analysis, including a generalized discussion of analytic steps.

9.1 BASIC CONCEPTS

The general purpose of the prospective, or *ex ante*, analysis discussed in the previous chapters of this guidance is to determine whether the benefits of the regulation are likely to exceed costs (i.e., whether benefits minus costs, or net benefits, are positive) and to identify the regulatory alternative likely to generate the largest net benefits. Figure 9.1 identifies several ways in which subsequent retrospective, or *ex post*, analysis of benefits and costs may be useful.[120]

FIGURE 9.1. USES OF RETROSPECTIVE BENEFIT COST ANALYSIS

1. Evaluate whether existing regulations continue to be justified in economic terms (i.e., produce positive net benefits).
2. Support identification of changes to existing regulations that will decrease their costs or increase their benefits.
3. Provide insight into the accuracy of *ex ante* estimates of regulatory benefits and costs, particularly whether they tend to be over- or underestimated.
4. Identify ways to improve the accuracy of future cost-benefit analyses.

A primary goal is to assess whether the regulation has achieved the desired outcome. For example, if its purpose was to reduce new cases of heart disease, analysts would seek empirical evidence of this impact. While potentially difficult to obtain, this information is a necessary to determine whether net benefits are positive.

Additionally, retrospective benefit-cost analysis "can help identify specific regulations that are ripe for regulatory reform, since their benefit-cost balance may be more or less favorable than originally expected" (OMB 2005). Importantly, OMB notes that "a validation study designed to determine the accuracy of *ex ante*

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[118] Aldy (2014) discusses the historical development of the retrospective review process within the Federal government and potential improvements.

[119] See the HHS website for the 2011 plan (http://www.hhs.gov/open/execorders/13563) as well as updates and an opportunity for public input regarding which regulations to review.

[120] This discussion is based largely on OMB (2005); more information is provided in subsequent reports such as OMB (2011c).

estimates does not by itself provide full guidance on the desirability of reforming the existing regulation" (OMB 2005, p. 41). For example, regulated entities may have incurred costs that will not be recovered if the regulation is retracted.[121]

Retrospective analysis may also inform the modification of an existing regulation with the goal of increasing its net benefits, regardless of whether net benefits are positive or negative as currently implemented. New information about key assumptions or inputs may suggest opportunities for optimizing the regulation.

After an agency has completed retrospective review of multiple regulations, it can identify whether it has a tendency to systematically over- or underestimate costs or benefits, and the extent to which over- or underestimation is attributable to various factors.[122] This information might highlight the need for additional uncertainty analysis, as well as ways in which future analyses can be improved.[123] It might also provide insight into how much weight should be granted to the cost-benefit analysis in the decision-making process as agencies promulgate new regulations (OMB 2005).

Finally, such information may identify ways to improve the accuracy of future *ex ante* analyses. For example, it may demonstrate that agencies routinely underestimate the ability of regulated entities to reduce costs as they gain experience with a particular regulation.[124] In certain cases, a regulation may motivate affected entities to go beyond the required compliance standards, resulting in additional health or other improvements not included in *ex ante* benefits estimates.[125] A better understanding of how affected entities respond to regulation will help improve the accuracy of future *ex ante* analysis.[126]

9.2 GENERAL APPROACH

In general, analysts should pursue retrospective benefit-cost analysis for those economically significant regulations identified in the HHS *Plan for Retrospective Review* where the need for regulatory reform is not obvious for other reasons (such as where the regulation requires obsolete technology) and where available data allow for meaningful assessment of impacts. Below, we first discuss challenges to estimating the effect of the regulation and addressing the time frame over which the impacts occurred, then describe the overall framework for the analysis.

9.2.1 ESTIMATING THE IMPACT OF THE REGULATION

The public or decision-makers may presume that retrospective analysis will be more accurate than prospective analysis because analysts can simply "tally" benefits and costs that have actually occurred. In other words, retrospective analysis may be perceived as a simple accounting exercise. However, correctly measuring incremental effects on a retrospective basis presents similar challenges to estimating impacts prospectively and is also subject to substantial uncertainty. The key challenge to *ex post* analysis is isolating the incremental effects

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[121] Such incurred, or "sunk" costs have zero opportunity costs because these resources have already been used and cannot be used again. When the analytic goal is to determine whether to revise or vacate an existing regulation, and significant costs have been incurred, a prospective analysis of retracting the existing regulation may be more appropriate than a retrospective evaluation.

[122] An agency might also use retrospective review to better understand the cumulative effect of multiple regulations aimed at reducing the same risk.

[123] For review of the results of retrospective benefit-cost analyses of Federal regulations see, for example, Harrington et al. (2000), Harrington (2006), and Morgenstern (2015).

[124] A substantial body of literature on "learning by doing" examines declines in the per-unit cost of producing or using a new technology as experience with the technology increases over time, as discussed in Chapter 4 and EPA (2010).

[125] For example, in 2003, FDA promulgated a final regulation requiring that trans fatty acids be declared in the nutrition label of conventional foods and dietary supplements on a separate line immediately under the line for the declaration of saturated fatty acids. Subsequent review of industry compliance with the regulation revealed that the informational nature of the regulation and the desire to maintain market share for certain food products created incentives for the industry to find ways to reduce trans fatty acids in foods to a degree that exceeded FDA's expectations. As a result, *ex ante* estimates of costs and health benefits may have been understated.

[126] In addition to improving the accuracy of future *ex ante* analysis, a better understanding of how affected entities respond to regulations may identify more efficient methods of achieving similar policy objectives. For example, if analysts learn that assuming complete compliance with future regulations overstates actual compliance rates, they may determine that increasing enforcement resources for existing regulations will achieve better health outcomes for less cost than introducing additional regulations.

of the regulation. As with *ex ante* analysis, identifying incremental effects requires comparing two scenarios: the world with the regulation (the "incremental scenario") and the world without the regulation (the "baseline scenario" in *ex ante* analysis, as discussed in Chapter 2, or "counterfactual scenario" in *ex post* analysis).[127]

In *ex ante* analysis both scenarios occur in the future; neither is observed. Ideally, analysts do not assume that current conditions will persist in the future; the baseline is the evolution of the existing, observed world. Both the baseline and incremental scenarios are subject to significant uncertainty associated with assumptions about likely future health and economic conditions without the regulation, compliance with the regulation, and behavioral responses that may affect implementation (e.g., innovation by the regulated community).

In *ex post* analysis, uncertainty may be reduced because the world with the regulation (the incremental scenario) can be observed. What were included as probabilities or expected values in the *ex ante* analysis can be replaced with actual outcomes, to the extent that it is possible to separate the effects of the regulation from other factors. The agency may have data on compliance rates, or it may be able to obtain more accurate information on key assumptions, such as the number of units of a drug sold. In other cases, it may be difficult to separate the effects of the regulation from other factors. For example, the incidence of the health conditions addressed by the regulation may be rising or falling due to medical innovations, changing demographics, or other causes. The extent to which the regulation has accelerated a decrease in incidence, or offset what would have otherwise been an even larger increase, may be difficult to isolate, even using sophisticated statistical tools. Furthermore, analysts must still model the counterfactual scenario, which cannot be observed. Assumptions about what the world would have been like without the regulation introduce uncertainty to estimates of the incremental impacts.[128,129]

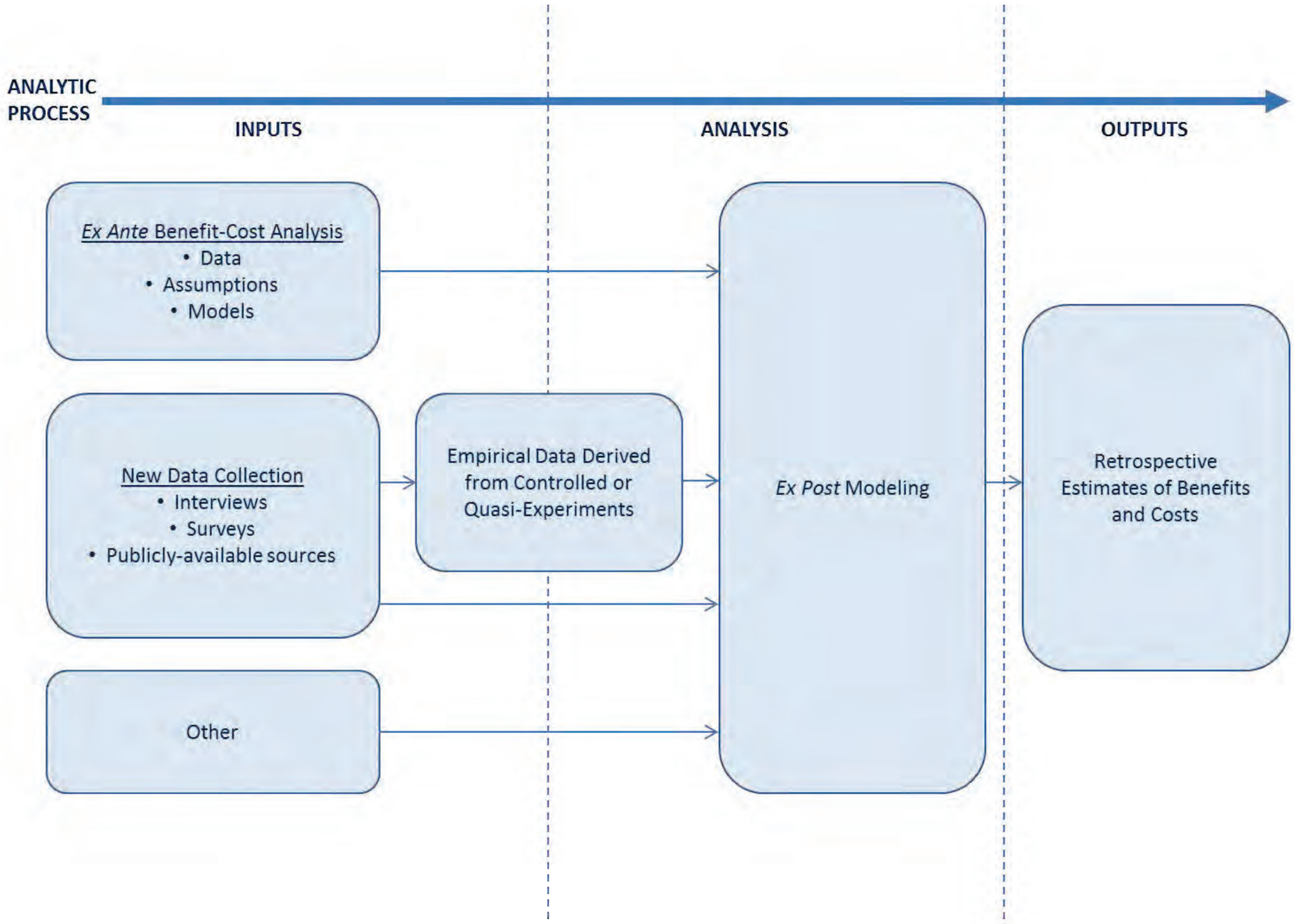
The major components of a retrospective benefit-cost analysis are the same as the RIA components illustrated in Figure 1.1. Figure 9.2 illustrates the process used to construct new models and highlights differences in the data and information potentially available for retrospective benefit-cost analysis. The process begins with the evaluation of existing information and the collection of new data. Relevant information may be obtained from a variety of sources, including the *ex ante* analysis previously developed in support of the regulation, newly available public information, surveys, or other sources. Retrospective analysis, like prospective analysis, is subject to the requirements of the PRA, which may limit an agency's ability to conveniently collect new data.

[127] The relevant comparison is the world with and without the regulation, not the world before and after the regulation is implemented. For example, a regulated entity's operating costs after a regulation takes effect may be influenced by market conditions or other factors unrelated to the regulation. Simply comparing costs before and after the regulation takes effect, without accounting for these other changes, could be misleading.

[128] *Ex ante* analysis estimates net benefits conditional on one or more sets of assumptions about the future, and sometimes uncertainty with regard to estimated net benefits may be aggregated over sets of future uncertain factors. In contrast, *ex post* analysis estimates net benefits conditional on specific realization of at least some of the *ex ante* uncertain factors. When using *ex post* analysis to judge the accuracy of *ex ante* estimates, this difference affects the interpretation and must be recognized.

[129] Many *ex ante* actions are undertaken to protect against uncertain adverse events. If the event does not occur, that does not necessarily mean that the regulation was unwarranted. For example, a vaccination policy does not necessarily have negative net benefits if the disease does not materialize; the insurance against possible disease provides its own benefit. Uncertainty about the likelihood of occurrence should be considered in the retrospective analysis as well as the prospective analysis.

FIGURE 9.2. RETROSPECTIVE ANALYSIS PROCESS



As indicated by the figure, data from two types of experiments might be available for these analyses: controlled or quasi-experiments. In the best case, the agency would design the regulation to allow for a controlled experiment, enabling analysts to empirically estimate the impact of the regulation with a high degree of confidence by comparing otherwise-identical treatment (i.e., subject to the regulation) and control (i.e., not subject to the regulation) groups.[130] This information on actual effects can replace assumptions about likely effects in the cost and benefit models. However, implementation of a controlled experiment is often at odds with regulatory design, which targets the populations in need of intervention or, for fairness, applies equally to everyone. Alternatively, in certain circumstances opportunities for natural or quasi-experimental designs, where natural randomization is exploited, may exist. For example, analysts may be able to identify unregulated comparison groups if (1) the regulation is phased in through time (new products are subject to the regulation while similar, older products are exempt); or (2) the regulation is not implemented uniformly across all geographic areas (e.g., implementation may differ across states).[131]

Such controlled or quasi-experiments may provide the best assessment of the actual effects of existing regulations because they are based on observed outcomes and data.[132] However, in practice, they may be too small in scale to be extrapolated to a national level, or the conditions necessary for successful experiments may be unavailable. For example, in many cases Federal regulations apply broadly to the general population. Thus, comparable control groups do not exist. Comparing populations through time may be more feasible; however, changes in underlying economic or health conditions may complicate such comparisons. Some of these challenges may be overcome using simple regression analysis or more sophisticated econometric modeling techniques.[133] In addition, regulations should be designed to ensure that monitoring or other data are available for use in future retrospective assessments.

The input data and additional analytic results are then used to update existing *ex ante* models or create new *ex post* models, as discussed in greater detail later in this chapter. At the conclusion of the process, decision-makers would use the results of the *ex post* modeling effort to evaluate the regulations. The process may be iterative as new data or insights are identified.

9.2.2 ADDRESSING THE TIMING OF THE IMPACTS

Below, we address two additional technical issues. They include defining the period of analysis and calculating present value and annualized impacts. While these issues are also relevant to prospective analysis, they may be addressed differently in retrospective analysis, depending on the period of interest.

Determining the time horizon: In retrospective analysis, defining the relevant time horizon is fairly simple. As with prospective analysis, the retrospective analysis should start in the year the impacts were first incurred, even if that period predates the effective date of the final regulation. For example, many regulated entities may incur costs in anticipation of upcoming regulations as they prepare to meet the regulation's effective date. These costs should be included in the analysis.

The end date is determined by the date when the retrospective analysis is undertaken or the most recent date for which retrospective data are available. To the extent that agencies wish to project impacts into the future based on new information collected in the retrospective analysis, additional prospective results should be clearly

[130] For a discussion of regulatory design intended to foster such experiments, see Greenstone (2009).

[131] For example, the National Traffic Highway Safety Administration (NHTSA) often issues standards applying only to new vehicles. Thus, it can estimate the efficacy of new safety equipment by comparing contemporaneous accident reports for new vehicles to similar records for older vehicles manufactured prior to the effective date of the final regulation (Lutter 2013).

[132] For two examples of these types of experiments conducted in the context of public health policy, see Newhouse and the Insurance Experiment Group (1996) and Baicker et al. (2013).

[133] For an informative discussion of the use of controlled and quasi-experiments in policy evaluation and the statistical analysis of such empirical data, see HM Treasury (2011), Chapter 9. For additional guidance on the design and conduct of such experiments, see Box et al. (2005).

separated and reported, as prospective analysis requires a different set of assumptions to address the future baseline and incremental scenarios.

Where the benefits and costs of a regulation are expected to occur unevenly through time, the analysts should consider the full time period over which the regulation was implemented. Longer timeframes may be particularly important when positive health impacts are not expected to be measurable until many years after the regulation goes into effect. In such cases, a longer timeframe ensures that all significant one-time benefits and costs are captured in the analysis. However, if benefits and costs are likely to remain constant through the period of the analysis, it may be sufficient to model impacts for a single year.[134]

Finally, if the agency wishes to compare the results of *ex ante* and *ex post* analyses, it must model the same time periods. However, this may not always be possible, particularly if the agency reviews the regulation within the first few years of implementation. In such cases, analysts should adjust *ex ante* estimates to exclude years not analyzed in the *ex post* analysis. Agencies should also ensure that the identical time periods are covered when comparing *ex ante* and *ex post* estimates of annualized impacts.

Calculating present value and annualized impacts: Regardless of whether impacts occur in the future or the past, time preferences matter. Resources allocated to compliance in prior years could have been used for other purposes. Benefits accrued earlier are generally more valuable than those accrued later. If analysts are interested in comparing the results of the retrospective analysis to the prospective analysis, they should report benefits and costs in present value terms using the same base year (see Chapter 5). Generally, the starting point (base year) is the year the regulation went into effect or the first year costs or benefits were incurred. Alternatively, impacts may be reported on an annualized basis. In either case, the stream of benefits and costs should also be reported by year and in constant, undiscounted dollars for those years.

9.2.3 FRAMING THE *EX POST* MODELING EFFORT

Earlier in this chapter, Figure 9.2 describes the general components of retrospective analysis, including inputs, analysis, and outputs. This section provides additional discussion of the choices analysts face during the analysis, particularly the *ex post* modeling effort. Generally, analysts should follow a phased approach to ensure that their work is carefully focused and useful for decision-making, following the steps listed in Figure 9.3 as discussed below.

Prior to initiating any retrospective modeling effort, analysts should consider the purpose of the effort, as the goal may affect the content of the analysis (see Figure 9.1). Based on that purpose, they should develop reasonable stopping rules to define the scope of the analysis. These rules are designed to focus analysts on answering the pertinent question related to a particular regulation, while avoiding unnecessary and expensive data collection and analysis.

Analysts should follow a stepwise progression: (1) simple screening analysis; (2) revisions to existing models developed for the *ex ante* regulatory analysis; and (3) entirely new modeling efforts, as indicated in greater detail in Figure 9.3. For example, if the purpose of the effort is to determine whether the benefits of a regulation exceed costs, and a simple screening analysis can answer this question, additional modeling efforts may not be necessary.

[134] Such a situation seems unlikely given continued changes in the size of the U.S. economy. But per capita effects might be roughly constant and reporting them would be perhaps as useful as reporting totals.

FIGURE 9.3. SUGGESTED STEPS FOR *EX POST* MODELING

LEVEL OF EFFORT	STEPS
Lowest ⇩	***Screening Analysis*** • Conduct case studies of incurred costs or benefits. • Conduct a simple bounding analysis with assumptions based on observed data.
⇩ ⇩ ⇩	***Adjust Existing Ex Ante Model Assumptions and Data*** In addition to the above screening tools, • Identify the key assumptions or data sources influencing the impact estimates in the *ex ante* model. • Focus retrospective research efforts on refining these assumptions and data, such as through natural or controlled experiments or other data collection efforts. • Update counterfactual and incremental scenarios using the existing model and this new information. • Evaluate the validity of existing models and whether they will achieve the goals of the retrospective analysis (e.g., whether they accurately depict the response of the regulated community).
⇩ **Highest**	***Construct a New Model*** In addition to, or in place of, adjustments to the *ex ante* model, • Use existing and new information to construct a new model of impacts. • Ensure the new model captures missing categories of benefits and costs or unanticipated responses by the affected community.

If analysts are interested not just in whether the regulation was effective, but also in the accuracy of the *ex ante* cost and benefit estimates, additional modeling may be required. They should first review the key assumptions or data sources driving the results of the *ex ante* analysis, particularly if the appropriateness of these is uncertain and they substantially affect the results. Analysts should focus their research on refining or updating these key factors.[135] Variations of the original *ex ante* models could be used to estimate the incremental change compared with the counterfactual scenario. However, such an approach assumes that the original models accurately characterize the implementation of the regulation and linkages to resulting benefits and costs.[136]

In some cases, through interviews with affected entities, additional data collection, or the results of controlled or quasi-experiments, analysts may determine that the *ex ante* models did not accurately characterize the impacts of the regulation. For example, compliance costs may be lower than anticipated if affected entities develop innovative methods of compliance, or improvements in overall productivity reduce all costs, including compliance costs. Or underlying market conditions may fundamentally change, making substitute sources of

[135] It is particularly helpful if the original *ex ante* analysis clearly identifies key assumptions and sources of uncertainty. Sensitivity analysis can be used to demonstrate the importance of each uncertain variable.

[136] A particularly well-known example of a regulation where the *ex ante* models did not accurately predict the behavioral response of the regulated community is the case of EPA's regulation of sulfur dioxide (SO_2) emissions. As described in Harrington et al. (2000), emissions reductions exceeded expectations for several reasons, including greater than expected efficacy of pollution control equipment, innovation by the regulated community, and changes in market conditions. The SO_2 regulation illustrates circumstances that would necessitate new cost and benefit modeling to accurately estimate the net benefits of the regulation.

goods or materials available to offset costs or benefits. In other cases, the agency may learn that key categories of benefits and costs were omitted from the original analysis. Based on this new information, analysts may decide to develop new models of benefits and costs.

In sum, conducting retrospective analysis requires thinking carefully about its goals. In some cases, revisiting the prospective analysis from an *ex post* perspective will provide important insights into the benefits and costs of the regulation. In other cases, prospective analysis of the benefits and costs of eliminating or modifying the regulation may be useful – instead of, or in addition to, the *ex post* analysis. In either case, the level of effort should be tailored to the purpose of the review.

Appendix A
Agency Checklist: Regulatory Impact Analysis (OMB 2010)

This appendix replicates OMB's 2010 Checklist, which is also available at: https://www.whitehouse.gov/omb/inforeg_regpol_agency_review.

With this document, the Office of Information and Regulatory Affairs is providing a checklist to assist agencies in producing RIAs, as required for economically significant rules by Executive Order 12866 and OMB *Circular A-4*.

Nothing herein alters, adds to, or reformulates existing requirements in any way. Moreover, this checklist is limited to the requirements of Executive Order 12866 and Circular A-4; it does not address requirements imposed by other authorities, such as the National Environmental Policy Act, the Regulatory Flexibility Act, the Unfunded Mandates Reform Act, the Paperwork Reduction Act, and various Executive Orders that require analysis. Executive Order 12866 and Circular A-4, as well as those other authorities, should be consulted for further information.

Checklist for Regulatory Impact Analysis:

- Does the RIA include a reasonably detailed description of the **need for the regulatory action**?[1,2]
- Does the RIA include an explanation of how the regulatory action will **meet that need**?[3]
- Does the RIA use an appropriate **baseline** (i.e., best assessment of how the world would look in the absence of the proposed action)?[4]
- Is the information in the RIA based on **the best reasonably obtainable scientific, technical, and economic information** and is it presented in an **accurate, clear, complete, and unbiased manner**?[5]
- Are the data, sources, and methods used in the RIA provided to the public **on the Internet** so that a qualified person can reproduce the analysis?[6]
- To the extent feasible, does the RIA quantify and monetize the anticipated **benefits** from the regulatory action?[7,8]
- To the extent feasible, does the RIA quantify and monetize the anticipated **costs**?[9]
- Does the RIA explain and support **a reasoned determination that the benefits of the intended regulation justify its costs** (recognizing that some benefits and costs are difficult to quantify)?[10]
- Does the RIA assess the **potentially effective and reasonably feasible alternatives**?[11]
    - Does the RIA assess the benefits and costs of different regulatory provisions separately if the rule includes a number of distinct provisions?[12]
    - Does the RIA assess at least one alternative that is less stringent and at least one alternative that is more stringent?[13]
    - Does the RIA consider setting different requirements for large and small firms?[14]
- Does the preferred option have the highest **net benefits** (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity), unless a statute requires a different approach? [15]
- Does the RIA include an explanation of why the planned regulatory action is **preferable** to the identified potential alternatives?[16]
- Does the RIA use appropriate **discount rates** for benefits and costs that are expected to occur in the future?[17]
- Does the RIA include, if and where relevant, an appropriate **uncertainty analysis**?[18]

- Does the RIA include, if and where relevant, a separate description of **distributive impacts** and **equity**?[19]
  - Does the RIA provide a description/accounting of transfer payments?[20]
  - Does the RIA analyze relevant effects on disadvantaged or vulnerable populations (e.g., disabled or poor)?[21]
- Does the analysis include a clear, plain-language **executive summary**, including an **accounting statement** that summarizes the benefit and cost estimates for the regulatory action under consideration, including the qualitative and non-monetized benefits and costs?[22]
- Does the analysis include a clear and transparent **table** presenting (to the extent feasible) anticipated benefits and costs (quantitative and qualitative)?[23]

NOTES

1. Required under Executive Order 12866, Section 6(a)(3)(B)(i): "The text of the draft regulatory action, together with a reasonably detailed description of the need for the regulatory action and an explanation of how the regulatory action will meet that need."
2. Circular A-4 states: "If the regulation is designed to correct a significant market failure, you should describe the failure both qualitatively and (where feasible) quantitatively." (P. 4)
3. See note 1 above.
4. Circular A-4 states: "You need to measure the benefits and costs of a rule against a baseline. This baseline should be the best assessment of the way the world would look absent the proposed action… In some cases, substantial portions of a rule may simply restate statutory requirements that would be self-implementing, even in the absence of the regulatory action. In these cases, you should use a pre-statute baseline." (P. 15-16)
5. Circular A-4 states: "Because of its influential nature and its special role in the rulemaking process, it is appropriate to set minimum quality standards for regulatory analysis. You should provide documentation that the analysis is based on the best reasonably obtainable scientific, technical, and economic information available… you should assure compliance with the Information Quality Guidelines for your agency and OMB's Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies..." (P. 17). The IQ Guidelines (paragraph V.3.a) define objectivity to include "whether disseminated information is being presented in an accurate, clear, complete, and unbiased manner."
   http://www.whitehouse.gov/omb/assets/omb/fedreg/reproducible2.pdf
6. Circular A-4 states: "A good analysis should be transparent and your results must be reproducible. You should clearly set out the basic assumptions, methods, and data underlying the analysis and discuss the uncertainties associated with the estimates. A qualified third party reading the analysis should be able to understand the basic elements of your analysis and the way in which you developed your estimates. To provide greater access to your analysis, you should generally post it, with all the supporting documents, on the internet so the public can review the findings." (P. 17). OMB IQ Guidelines (paragraph V.3.b.ii) further states: "If an agency is responsible for disseminating influential scientific, financial, or statistical information, agency guidelines shall include a high degree of transparency about data and methods to facilitate the reproducibility of such information by qualified third parties."
7. Required under Executive Order 12866, Section 6(a)(3)(C)(i): "An assessment, including the underlying analysis, of benefits anticipated from the regulatory action (such as, but not limited to, the promotion of the efficient functioning of the economy and private markets, the enhancement of health and safety, the protection of the natural environment, and the elimination or reduction of discrimination or bias) together with, to the extent feasible, a quantification of those benefits."

8. Circular A-4 states: "You should monetize quantitative estimates whenever possible. Use sound and defensible values or procedures to monetize benefits and costs, and ensure that key analytical assumptions are defensible. If monetization is impossible, explain why and present all available quantitative information." (P. 19). Circular A-4 also offers a discussion of appropriate methods for monetizing benefits that might not easily be turned into monetary equivalents.

9. Required under Executive Order 12866, Section 6(a)(3)(C)(ii): "An assessment, including the underlying analysis, of costs anticipated from the regulatory action (such as, but not limited to, the direct cost both to the government in administering the regulation and to businesses and others in complying with the regulation, and any adverse effects on the efficient functioning of the economy, private markets (including productivity, employment, and competitiveness), health, safety, and the natural environment), together with, to the extent feasible, a quantification of those costs;" See also note 6 above.

10. Executive Order 12866, Section 1(b)(6) states that to the extent permitted by law, "[e]ach agency shall assess both the costs and the benefits of the intended regulation and, recognizing that some costs and benefits are difficult to quantify, propose or adopt a regulation only upon a reasoned determination that the benefits of the intended regulation justify its costs." As Executive Order 12866 recognizes, a statute may require an agency to proceed with a regulation even if the benefits do not justify the costs; in such a case, the agency's analysis may not show any such justification.

11. Required under Executive Order 12866, Section 6(a)(3)(C)(iii): "An assessment, including the underlying analysis, of costs and benefits of potentially effective and reasonably feasible alternatives to the planned regulation, identified by the agencies or the public (including improving the current regulation and reasonably viable nonregulatory actions)..."

12. Circular A-4 states: "You should analyze the benefits and costs of different regulatory provisions separately when a rule includes a number of distinct provisions." (P. 17)

13. Circular A-4 states: "you generally should analyze at least three options: the preferred option; a more stringent option that achieves additional benefits (and presumably costs more) beyond those realized by the preferred option; and a less stringent option that costs less (and presumably generates fewer benefits) than the preferred option." (P. 16)

14. Circular A-4 states: "You should consider setting different requirements for large and small firms, basing the requirements on estimated differences in the expected costs of compliance or in the expected benefits. The balance of benefits and costs can shift depending on the size of the firms being regulated. Small firms may find it more costly to comply with regulation, especially if there are large fixed costs required for regulatory compliance. On the other hand, it is not efficient to place a heavier burden on one segment of a regulated industry solely because it can better afford the higher cost. This has the potential to load costs on the most productive firms, costs that are disproportionate to the damages they create. You should also remember that a rule with a significant impact on a substantial number of small entities will trigger the requirements set forth in the Regulatory Flexibility Act. (5 U.S.C. 603(c), 604)." (P. 8)

15. Executive Order 12866, Section 1(a) states: "agencies should select those approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity) unless a statute requires another regulatory approach."

16. Required under Executive Order 12866, Section 6(a)(3)(C)(iii): "An assessment, including the underlying analysis, of costs and benefits of potentially effective and reasonably feasible alternatives to the planned regulation, identified by the agencies or the public (including improving the current regulation and reasonably viable nonregulatory actions), and an explanation why the planned regulatory action is preferable to the identified potential alternatives."

17. Circular A-4 contains a detailed discussion, generally calling for discount rates of 7 percent and 3 percent for both benefits and costs. It states: “Benefits and costs do not always take place in the same time period. When they do not, it is incorrect simply to add all of the expected net benefits or costs without taking account of when they actually occur. If benefits or costs are delayed or otherwise separated in time from each other, the difference in timing should be reflected in your analysis.... For regulatory analysis, you should provide estimates of net benefits using both 3 percent and 7 percent.... If your rule will have important intergenerational benefits or costs you might consider a further sensitivity analysis using a lower but positive discount rate in addition to calculating net benefits using discount rates of 3 and 7 percent.” (PP. 31, 34, 36)

18. Circular A-4 provides a detailed discussion. Among other things, it states: “Examples of quantitative analysis, broadly defined, would include formal estimates of the probabilities of environmental damage to soil or water, the possible loss of habitat, or risks to endangered species as well as probabilities of harm to human health and safety. There are also uncertainties associated with estimates of economic benefits and costs, such as the cost savings associated with increased energy efficiency. Thus, your analysis should include two fundamental components: a quantitative analysis characterizing the probabilities of the relevant outcomes and an assignment of economic value to the projected outcomes.” (P. 40). Circular A-4 also states: “You should clearly set out the basic assumptions, methods, and data underlying the analysis and discuss the uncertainties associated with the estimates.” (P. 17)

19. Executive Order 12866, Section 1(b)(5) states; “When an agency determines that a regulation is the best available method of achieving the regulatory objective, it shall design its regulations in the most cost-effective manner to achieve the regulatory objective. In doing so, each agency shall consider incentives for innovation, consistency, predictability, the costs of enforcement and compliance (to the government, regulated entities, and the public), flexibility, *distributive impacts*, and *equity*” (emphasis added). Circular A-4 states: “The term ‘distributional effect’ refers to the impact of a regulatory action across the population and economy, divided up in various ways (e.g., income groups, race, sex, industrial sector, geography)… Your regulatory analysis should provide a separate description of distributional effects (i.e., how both benefits and costs are distributed among sub-populations of particular concern) so that decision makers can properly consider them along with the effects on economic efficiency… Where distributive effects are thought to be important, the effects of various regulatory alternatives should be described quantitatively to the extent possible, including the magnitude, likelihood, and severity of impacts on particular groups.” (P. 14)

20. Circular A-4 states: “Distinguishing between real costs and transfer payments is an important, but sometimes difficult, problem in cost estimation. . . . Transfer payments are monetary payments from one group to another that do not affect total resources available to society. . . . You should not include transfers in the estimates of the benefits and costs of a regulation. Instead, address them in a separate discussion of the regulation's distributional effects.” (P. 14)

21. Circular A-4 states: “Your regulatory analysis should provide a separate description of distributional effects (i.e., how both benefits and costs are distributed among sub-populations of particular concern) so that decision makers can properly consider them along with the effects on economic efficiency. Executive Order 12866 authorizes this approach. Where distributive effects are thought to be important, the effects of various regulatory alternatives should be described quantitatively to the extent possible, including the magnitude, likelihood, and severity of impacts on particular groups.” (P. 14)

22. Circular A-4 states: “Your analysis should also have an executive summary, including a standardized accounting statement.” (P. 3). OMB recommends that: “Regulatory analysis should be made as transparent as possible by a prominent and accessible executive summary—written in a “plain language” manner designed to be understandable to the public—that outlines the central judgments that support

regulations, including the key findings of the analysis (such as central assumptions and uncertainties)…If an agency has analyzed the costs and benefits of regulatory alternatives to the planned action (as is required for economically significant regulatory actions), the summary should include such information." See *2010 Report to Congress on the Benefits and Costs of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities*, page 51. Available at: http://www.whitehouse.gov/sites/default/files/omb/legislative/reports/2010_Benefit_Cost_Report.pdf

23. Circular A-4 states: "You need to provide an accounting statement with tables reporting benefit and cost estimates for each major final rule for your agency." (P. 44). Circular A-4 includes an example of a format for agency consideration. OMB recommends "that agencies should clearly and prominently present, in the preamble and in the executive summary of the regulatory impact analysis, one or more tables summarizing the assessment of costs and benefits required under Executive Order 12866 Section 6(a)(3)(C)(i)-(iii). The tables should provide a transparent statement of both quantitative and qualitative benefits and costs of the proposed or planned action as well as of reasonable alternatives. The tables should include all relevant information that can be quantified and monetized, along with relevant information that can be described only in qualitative terms. It will often be useful to accompany a simple, clear table of aggregated costs and benefits with a separate table offering disaggregated figures, showing the components of the aggregate figures. To the extent feasible in light of the nature of the issue and the relevant data, all benefits and costs should be quantified and monetized. To communicate any uncertainties, we recommend that the table should offer a range of values, in addition to best estimates, and it should clearly indicate impacts that cannot be quantified or monetized. If nonquantifiable variables are involved, they should be clearly identified. Agencies should attempt, to the extent feasible, not merely to identify such variables but also to signify their importance." See *2010 Report to Congress on the Benefits and Costs of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities*, page 51. Available at: http://www.whitehouse.gov/sites/default/files/omb/legislative/reports/2010_Benefit_Cost_Report.pdf

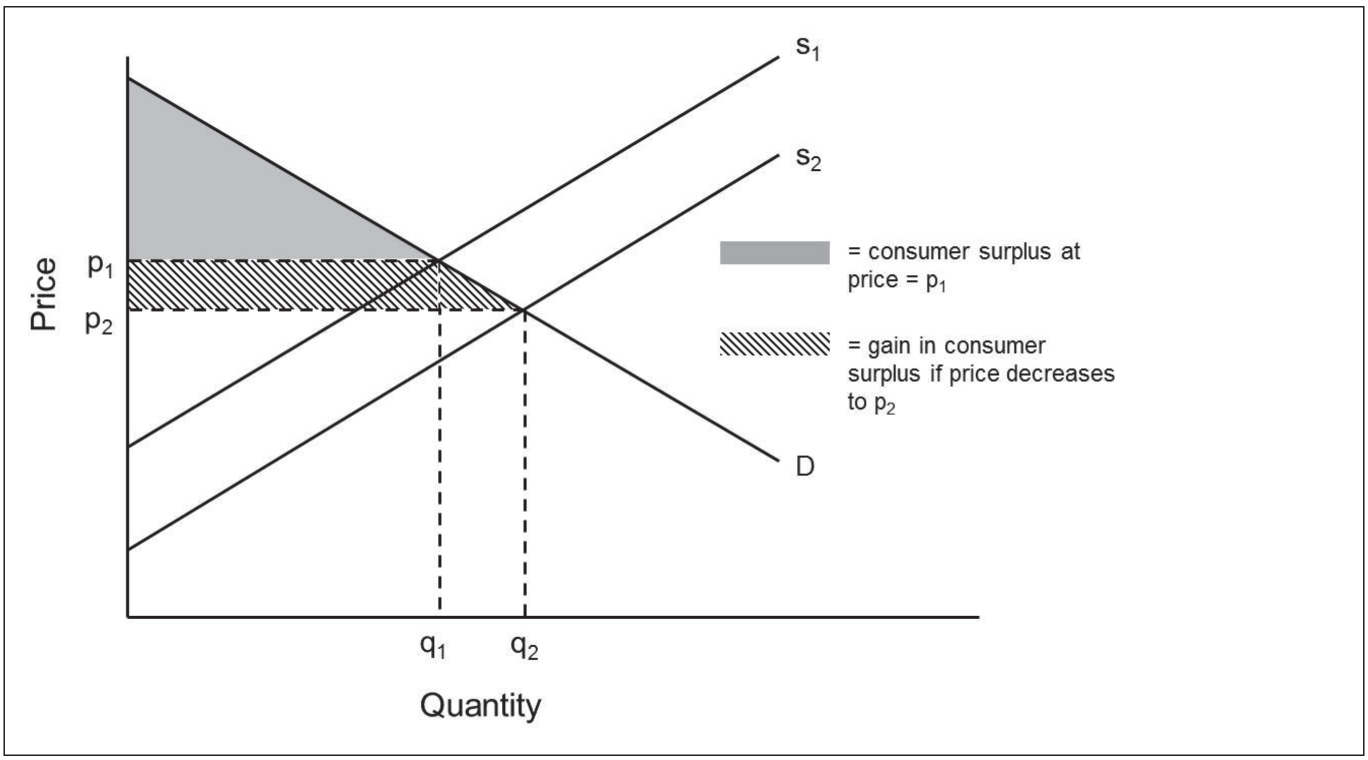
Appendix B

Consumer and Producer Surplus

As discussed in Chapter 3, a key assumption that underlies benefit-cost analysis is that benefit values are determined by the change in the amount by which aggregate WTP exceeds the market price, or “consumer surplus.” When WTP exceeds price, the individual benefits from the fact that he or she can acquire the good or service for less than his or her willingness to pay. If price exceeds WTP, the individual would not purchase the good or service, choosing to use the money for other things. The difference between WTP and price can be aggregated across individuals to determine the consumer surplus associated with different price levels. Consumers generally benefit from price decreases, because WTP then exceeds price by a larger amount, and vice-versa.

This relationship is illustrated by Figure B.1. The horizontal axis represents the quantity of the good (q), the vertical axis represents its price (p). The market demand curve (D) indicates both consumers’ WTP at each quantity and the quantity that would be purchased at each price.[137] Similarly, the supply curve (S) indicates both the marginal cost of supply at each quantity and the quantity that would be supplied at each price. The equilibrium market price is determined by where the two curves intersect. At this point, only consumers whose WTP exceeds the price purchase the good, and only producers whose cost of supply is less than the price produce it. For example, at price p_1, consumers would purchase quantity q_1. The shaded area above the price line and below the demand curve indicates the amount by which WTP exceeds price; i.e., consumer surplus at price p_1.

FIGURE B.1. CHANGE IN CONSUMER SURPLUS DUE TO A PRICE DECREASE



[137] Depending on the good or service, the prices represented in this schedule may reflect time costs or other factors that influence demand, in addition to the “sticker price” viewed by the consumer. Demand curves can also be developed for nonmarket goods, using the techniques described in Chapter 3 to estimate WTP.

If the price decreases, the quantity demanded rises as some consumers choose to purchase the good at the lower price rather than buying other goods or services. If changes in supply lead price to drop from p_1 to p_2, consumers would increase their purchases to quantity q_2.

When the price falls from p_1 to p_2, consumers benefit in two ways. First, they pay less for the q_1 units they continue to buy. Second, they buy $q_2 – q_1$ additional units for which WTP exceeds p_2 but does not exceed p_1. (The size of the increase in q is often summarized by the "demand elasticity," defined as the proportional change in q divided by the proportional change in p.) The area marked with diagonal lines indicates the gain in consumer surplus that results from the price decrease from p_1 to p_2.[138]

Similar concepts apply to producers. Regulatory compliance costs may affect the price and quantity of goods exchanged in the market, leading to changes in producer surplus. These relationships are illustrated by Figure B.2 for a competitive market.[139] In this case, we illustrate a cost increase that results from compliance with a new regulation. As in the earlier figure, the horizontal axis represents the quantity of the good (q) and the vertical axis represents its price (p); the market demand curve (D) indicates both consumers' WTP at each quantity and the quantity that would be purchased at each price; the supply curve (S) indicates both the marginal cost of supply at each quantity and the quantity that would be supplied at each price; and the equilibrium market price is determined by where the supply and demand curves intersect.

If the cost of supplying the good increases as a result of the regulation, the supply curve shifts upwards, from s_1 to s_2, reducing consumer surplus (the area between the demand curve and the price line). Producer surplus, which reflects the difference between the market price and supply costs (the area above the supply curve and below the price line), also decreases. For example, at price p_1 producers will supply quantity q_1. When supply costs increase, producers will provide a smaller quantity for each price and demand a higher price for each quantity. Thus the market price will increase to p_2 and the quantity sold will decrease to q_2.

The area bounded by the two supply curves and the new quantity line represents the increased cost of producing the quantity that is demanded at the new price.[140] In addition, the reduction in output results in a deadweight loss represented by the solid triangle, indicating forgone net benefits. This deadweight loss is part of the costs of the regulation.[141] Thus the net reduction in the total surplus (consumer plus producer) is a real cost to society. The question for analysts is whether these costs are greater or less than aggregate WTP for the regulation's benefits.

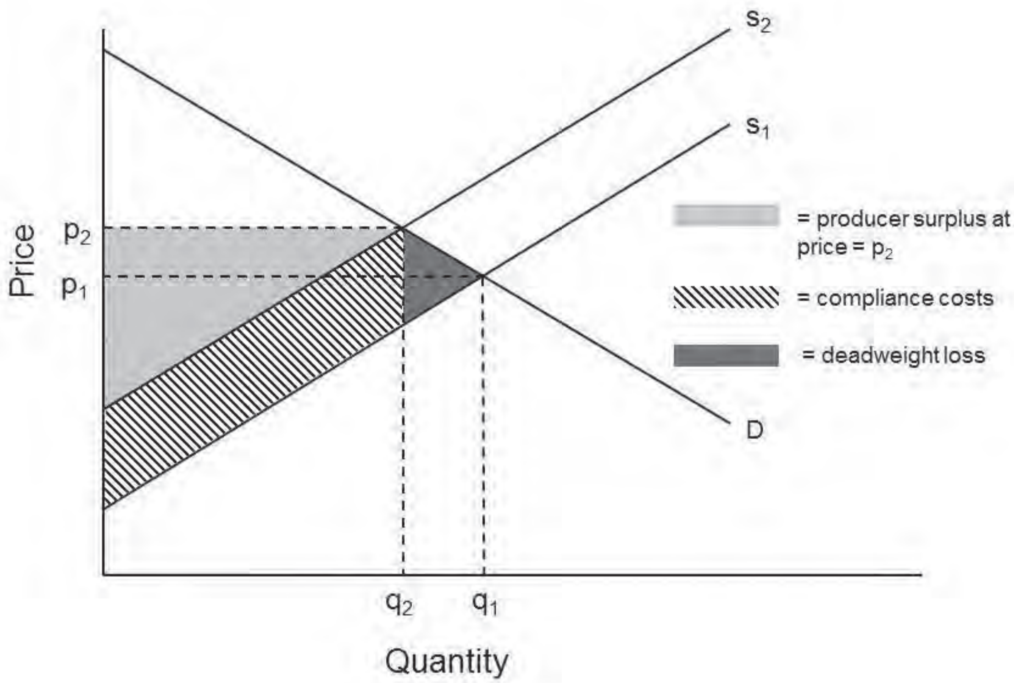
[138] When the price falls, some consumers who purchase the good at p_1 might purchase more units and some who do not purchase it at p_1 may purchase at the lower price p_2. In this case, the graph displays aggregate demand by all consumers; it does not indicate what quantity each consumer purchases. A similar graph could be drawn for an individual consumer.

[139] For a more detailed discussion of these concepts, see Boardman et al. (2011).

[140] As noted elsewhere, the real resource cost of producing a good may differ from the supply cost when the resource costs are not equal to the private costs, due to externalities, taxes, subsidies, or monopoly producers.

[141] Note that the deadweight loss results from changes in both producer and consumer surplus.

FIGURE B.2. CHANGE IN PRODUCER SURPLUS DUE TO A COST INCREASE



Appendix C

Methods for Estimating QALYs

As discussed in Chapter 3, estimating QALYs involves first determining the effect of a health state on HRQL, then multiplying HRQL by the duration of the health state. While the HRQL associated with a health state is likely to vary among individuals, in practice a common value is typically used for each state, representing a population average. This appendix introduces methods for estimating HRQL; more information on the implementation of these methods and their advantages and limitations is provided in Institute of Medicine (2006).

HRQL can be estimated directly or indirectly. Commonly used direct methods include the standard gamble, time tradeoff, and visual analog scale, administered in interviews or a survey. The standard gamble approach asks respondents to compare living the rest of their life (T years) in the health state of interest with a gamble between living the rest of their life in full health (with probability p) and immediate death (with probability 1 – p). The probability p* at which the individual is indifferent is his or her HRQL for that health state. This follows because living the rest of his or her life in the specified health state yields p* T QALYs (i.e., T years weighted by an HRQL of p*) and the gamble provides an expected value of p* T QALYs (i.e., a p* chance of T QALYs (T years weighted by an HRQL of 1) plus a complementary chance of zero QALYs (immediate death)).

The time tradeoff approach asks respondents to compare living the rest of their life (T years) in the health state of interest with living a shorter period (qT years) in full health, followed by death. The value q* at which the individual is indifferent is his or her HRQL for the health state. This follows because living T years with HRQL q* provides q* T QALYs, and living q* T years in full health also provides q* T QALYs.

The visual analog scale does not require a comparison of different future lives. It simply asks the individual to rate the health state of interest on a visual scale where one end is described as being as bad as dead and labeled 0, and the other is described as full health and labeled 100. (Alternatively, the individual may be asked to report a number between 0 and 100 rather than marking it on the scale.) HRQL is then defined as the response divided by 100.

An indirect method to estimate HRQL is to apply one of several generic HRQL indices, examples of which include the EurQol- (EQ)-5D, the Health Utilities Index (HUI), and the Quality of Well-Being (QWB) scale. Each describes health status by employing a classification system with several dimensions. In the case of the EQ-5D, these include mobility, self-care, usual activities, pain, and anxiety and depression. A particular health state is rated within each dimension; for example, as causing no, some, or extreme mobility problems. The HRQL associated with each health state is then calculated by applying a scoring function, developed by eliciting HRQL for some of the health states through a population survey using one of the direct methods described earlier. These indices have the advantage of standardizing the approach for describing each health state and providing a convenient method to calculate HRQL. The results will vary, however, depending on which index is applied, given differences in the attributes they include and in the scoring functions.

Once HRQL is determined for a particular health state, it is multiplied by the duration of that state to estimate the associated QALYs. The QALYs can then be summed across health states (e.g., acute and chronic phases) associated with a particular illness, and across the illnesses associated with a particular hazard. For regulatory analysis, health status with the regulation must be compared to health status in the absence of the regulation, which is likely to be less than full health. In particular, health status generally deteriorates with age, so that average HRQL for older individuals is generally less than 1.0 (see, for example, Hamner et al. 2006). Expected QALYs are calculated by weighting the HRQL experienced in each future year of life by the probability of living that year (i.e., by the survival curve). In addition, future QALYs are usually discounted using the same discount rates as for monetary values.

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Index

Glossary

Accounting Costs: Actual expenses plus depreciation of capital equipment (Chapter 4).

Annualized Value: The constant annual amount, which, if paid each year over a defined time period, has the same present value as a specified series of unequal payments over the same period (Chapter 5).

Baseline: Expected future conditions in the absence of a new regulation or other policy change (Chapter 2).

Benefits: For the purpose of HHS regulatory analysis, the value of the intended outcomes of a regulation or other policy, such as reductions in mortality or morbidity risks, as well as any countervailing effects on these outcomes, such as health risk increases. Note that analyses not subject to this guidance may use differing definitions when categorizing outcomes as benefits or costs (Chapter 2).

Benefit Transfer: The application of values from the available research to a policy context that differs in some respects from the context studied. Involves evaluating the quality of the research and its applicability to the policy context (Chapter 3).

Bounding Analysis: The application of reasonable high and low parameter values to determine the extent to which the analytic results might change given the likely variation in the values (Chapter 6).

Breakeven Analysis: The value of an unknown or uncertain parameter at which benefits and costs would be equal, indicating how large the value would need to be to bridge the gap between the quantified benefits and costs. Also referred to as “threshold” analysis (Chapter 6).

Capital Cost: The value of resources, including equipment, buildings, and land, that are not immediately consumed in the production process (Chapter 4).

Compliance Cost: The value of resources, including labor, capital, and materials, used to implement a regulation or other policy. Includes only those resources expended by the entities and individuals directly responsible for implementation; excludes impacts on prices or other market conditions (Chapter 4).

Consumer Price Index (CPI): An index maintained by the U.S. Bureau of Labor Statistics that indicates changes in the prices paid by consumers for a market basket of goods and services over time. May be used to adjust values measured in current dollars to a common dollar year so that analyses can be conducted in real dollars, avoiding the need to adjust for expected inflation (Chapter 5).

Consumer Surplus: The difference between the maximum an individual would be willing to pay for a good or service and the market price (Chapter 3, Appendix B).

Costs: For the purpose of HHS regulatory analysis, the value of the inputs required to implement a regulation or other policy, including labor, capital, and materials, as well as any offsetting savings. Note that analyses not subject to this guidance may use differing definitions when categorizing outcomes as benefits or costs (Chapter 2).

Deadweight Loss: The net loss in consumer and producer surplus that accrues when government intervention or other factors prevent the market from reaching a competitive equilibrium (Appendix B).

Discounting: The process for converting values that accrue in different years to their present value, to reflect individual time preferences and the value of investments forgone (Chapter 5).

Distribution: The allocation of benefits, costs, or net benefits across different population groups, defined, for example, by income level (Chapter 7).

Experiments: Comparison of outcomes across groups who are similar or identical except for their exposure to a regulation or other policy (Chapter 9).

Gross Domestic Product (GDP) Implicit Price Deflator: A measure reported by the U.S. Bureau of Economic Analysis that indicates the ratio of the market value of goods and services in current dollars to its the value in chained (constant) dollars. May be used to adjust values measured in current dollars to a common dollar year so that analyses can be conducted in real dollars, avoiding the need to adjust for expected inflation (Chapter 5).

General Equilibrium Models: Models that can be used to estimate the economy-wide impact of a regulation or other policy with large impacts (Chapter 4).

Health-Related Quality of Life (HRQL): A numerical indicator of health status estimated using a scale anchored at zero and one, where one corresponds to full health and zero corresponds to a state that is as bad as dead (Chapter 3, Appendix C).

Income Elasticity: The proportional change in price or quantity associated with a change in real income. When used in estimating the VSL, it indicates the proportional change in value (i.e., unit price) associated with an income change (Chapter 3).

Inflation: Economy-wide increases in prices (Chapter 5).

Net Benefits: The difference, benefits minus costs (Chapter 2).

Nominal Value: Values expressed in current-year dollars, reflecting the effects of both inflation and real changes in value over time (Chapter 5).

Opportunity Cost: The benefits of the best alternative use of specified resources, which is forgone when resources are used for one purpose and hence cannot be used for other purposes (Chapter 4).

Partial Equilibrium Models: Models that describe the effects of a regulation or other policy in one market, which can be used to estimate the impact on an industry or group of industries (Chapter 4).

Present Value: The value of a stream of benefits, costs, or net benefits discounted to reflect their value in a common year (Chapter 5).

Probabilistic Analysis: The use of distributions of parameter values to explore the effects of uncertainty on an analytic result. Often employs Monte Carlo simulation techniques, which involve taking multiple random draws from the distribution for each critical parameter, calculating the model output for each draw, and using the results to represent the distribution of the outcome measure (Chapter 6).

Producer Surplus: The difference between the revenue producers receive and their cost of production (Chapter 4, Appendix B).

Quality-Adjusted Life Year (QALY): A nonmonetary measure that integrates the duration and severity of illness. Calculated by multiplying the amount of time an individual spends in a health state by the HRQL associated with that state, and summing over health states (Chapter 3, Appendix C).

Real Value: Values adjusted to a common dollar year (constant dollars), removing the effects of inflation (Chapter 5).

Retrospective Analysis (*ex post*): Assessment of the impacts of a regulation or a policy after it has been implemented, looking back to compare its impacts to what might have otherwise occurred, in contrast to prospective (*ex ante*) analysis which involves predicting future impacts (Chapter 9).

Revealed Preference Methods: Estimation of values based on observed market prices or behaviors (Chapter 3).

Screening Analysis: Use of readily available information and simple assumptions to provide preliminary information on potential impacts; may aid in targeting future work (Chapter 2).

Sensitivity Analysis: Varying one or more key parameter values to explore the effects of uncertainty on the analytic results (Chapter 6).

Social cost: The sum of the opportunity costs associated with the implementation of a regulation or other policy (Chapter 4).

Standing: The definition of whose benefits and costs are to be counted in an analysis. For HHS regulatory analysis, generally includes all U.S. residents (Chapter 2).

Stated Preference Methods: Estimation of values based on surveys or other self-reported data (Chapter 3).

Statistical Cases: Risk changes summed over the affected population; for example, if 10,000 people each experience a risk reduction of 1 in 10,000, then one statistical case has been averted (Chapter 3).

Transfer Payment: Monetary payments between individuals or groups that do not affect the total resources available to society (Chapter 4).

Uncertainty: Lack of knowledge about a parameter value that could be addressed by more research (Chapter 6).

Value per Quality-Adjusted Life Year (QALY): The marginal rate of substitution between money in a defined period and health-adjusted life years remaining; often approximated by dividing a value per statistical life (VSL) estimate by expected remaining QALYs (Chapter 3).

Value per Statistical Life (VSL): The marginal rate of substitution between money in a defined time period and mortality risk; often approximated by dividing individual willingness to pay for a small risk change by the risk change (Chapter 3).

Value per Statistical Life Year (VSLY): The marginal rate of substitution between money in a defined period and life years remaining; often approximated by dividing a VSL estimate by remaining life expectancy (Chapter 3).

Variability: “Real world” heterogeneity of a parameter value (Chapter 6).

Willingness to Pay (WTP): The maximum amount of money an individual would exchange to obtain an improvement, given his or her budget constraints, such that his or her wellbeing is as good with the improvement and having made the payment as without (Chapter 3).

THE CONVERSATION

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Forceful words don't always result in strong action. AP Photo/Damian Dovarganes

Half of unvaccinated workers say they'd rather quit than get a shot – but real-world data suggest few are following through

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Are workplace vaccine mandates prompting some employees to quit rather than get a shot?

A hospital in Lowville, New York, for example, had to shut down its maternity ward when dozens of staffers left their jobs rather than get vaccinated. At least 125 employees at Indiana University Health resigned after refusing to take the vaccine.

And several surveys have shown that as many as half of unvaccinated workers insist they would leave their jobs if forced to get the shot, which has raised alarms among some that more mandates could lead to an exodus of workers in many industries. New York, for example, is preparing for an exodus of health care workers – and may even call in the National Guard to help – as its vaccine mandate takes effect on Sept. 27, 2021.

But how many will actually follow through?

Strong words

In June 2021, we conducted a nationwide survey, funded by the Robert Wood Johnson Foundation, that gave us a sample of 1,036 people who mirrored the diverse makeup of the U.S. We plan to publish the survey in October.

We asked respondents to tell us what they would do if “vaccines were required” by their employer. We prompted them with several possible actions, and they could check as many as they liked.

We found that 16% of employed respondents would quit, start looking for other employment or both if their employer instituted a mandate. Among those who said they were “vaccine hesitant” – almost a quarter of respondents – we found that 48% would quit or look for another job.

Other polls have shown similar results. A Kaiser Family Foundation survey put the share of workers who would quit at 50%.

Separately, we found in our survey that 63% of all workers said a vaccine mandate would make them feel safer.

Quieter actions

But while it is easy and cost-free to tell a pollster you’ll quit your job, actually doing so when it means losing a paycheck you and your family may depend upon is another matter.

And based on a sample of companies that already have vaccine mandates in place, the actual number who do resign rather than get the vaccine is much smaller than the survey data suggest.

Houston Methodist Hospital, for example, required its 25,000 workers to get a vaccine by June 7. Before the mandate, about 15% of its employees were unvaccinated. By mid-June, that percentage had dropped to 3% and hit 2% by late July. A total of 153 workers were fired or resigned, while another 285 were granted medical or religious exemptions and 332 were allowed to defer it.

At Jewish Home Family in Rockleigh, New Jersey, only five of its 527 workers quit following its vaccine mandate. Two out of 250 workers left Westminster Village in Bloomington, Illinois, and even in deeply conservative rural Alabama, a state with one of the lowest vaccine uptake rates, Hanceville Nursing & Rehab Center lost only six of its 260 employees.

Delta Airlines didn’t mandate a shot, but in August it did subject unvaccinated workers to a US$200 per month health insurance surcharge. Yet the airline said fewer than 2% of employees have quit over the policy.

And at Indiana University Health, the 125 workers who quit are out of 35,800 total employees, or 0.3%.

Making it easy

Past vaccine mandates, such as for the flu, have led to similar outcomes: Few people actually quit their jobs over them.

And our research suggests in public communications there are a few things employers can do to minimize the number of workers who quit over the policy.

It starts with building trust with employees. Companies should also make it as easy as possible to get vaccinated – such as by providing on-site vaccine drives, paid time off to get the shot and deal with side effects, and support for child care or transportation.

Finally, research shows it helps if companies engage trusted messengers including doctors, colleagues and family to share information on the vaccine.

In other words, vaccine mandates are unlikely to result in a wave of resignations – but they are likely to lead to a boost in vaccination rates.

This story was updated to include reference to New York health care vaccine mandate.

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SCIENCEINSIDER HEALTH

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but vaccination remains vital

Israelis who had an infection were more protected against the Delta coronavirus variant than those who had an already highly effective COVID-19 vaccine

26 AUG 2021 • 8:00 PM • BY MEREDITH WADMAN

A Jerusalem health care worker in January prepares a dose of the Pfizer-BioNTech vaccine designed to prevent COVID-19. AHMAD GHARABLI/AFP VIA GETTY IMAGES

SHARE:

A version of this story appeared in Science, Vol 373, Issue 6559.

The natural immune protection that develops after a SARS-CoV-2 infection offers considerably more of a shield against the Delta variant of the pandemic coronavirus than two doses of the Pfizer-BioNTech vaccine, according to a large Israeli study that some scientists wish came with a "Don't try this at home" label. The newly released data show people who once had a SARS-CoV-2 infection were much less likely than never-infected, vaccinated people to get Delta, develop symptoms from it, or become hospitalized with serious COVID-19.

The study demonstrates the power of the human immune system, but infectious disease experts emphasized that this vaccine and others for COVID-19 nonetheless remain highly protective against severe disease and death. And they caution that intentional infection among unvaccinated people would be extremely risky. "What we don't want people to say is: 'All right, I should go out and get infected, I should have an infection party,'" says Michel Nussenzweig, an immunologist at Rockefeller University who researches the immune response to SARS-CoV-2 and was not involved in the study. "Because somebody could die."

The researchers also found that people who had SARS-CoV-2 previously and received one dose of the Pfizer-BioNTech messenger RNA (mRNA) vaccine were more highly protected against reinfection than those who once had the virus and were still unvaccinated. The new work could inform discussion of whether previously infected people need to receive both doses of the Pfizer-BioNTech vaccine or the similar mRNA vaccine from Moderna. Vaccine mandates don't necessarily exempt those who had a SARS-CoV-2 infection already and the current U.S. recommendation is that they be fully vaccinated, which means two mRNA doses or one of the Johnson & Johnson adenovirus-based vaccine. Yet one mRNA dose might be enough, some scientists argue. And other countries including Germany, France, Italy, and Israel administer just one vaccine dose to previously infected people.

The study, conducted in one of the most highly COVID-19–vaccinated countries in the world, examined medical records of tens of thousands of Israelis, charting their infections, symptoms, and hospitalizations between 1 June and 14 August, when the Delta variant predominated in Israel. It's the largest real-world observational study so far to compare natural and vaccine-induced immunity to SARS-CoV-2, according to its leaders.

The research impresses Nussenzweig and other scientists who have reviewed a preprint of the results, posted yesterday on medRxiv. "It's a textbook example of how natural immunity is really better than vaccination," says Charlotte Thålin, a physician and immunology researcher at Danderyd Hospital and the Karolinska Institute who studies the immune responses to SARS-CoV-2. "To my knowledge, it's the first time [this] has really been shown in the context of COVID-19."

Still, Thålin and other researchers stress that deliberate infection among unvaccinated people would put them at significant risk of severe disease and death, or the lingering, significant symptoms of what has been dubbed Long Covid. The study shows the benefits of natural immunity, but "doesn't take into account what this virus does to the body to get to that point," says Marion Pepper, an immunologist at the University of Washington, Seattle. COVID-19 has already killed more than 4 million people worldwide and there are concerns that Delta and other SARS-CoV-2 variants are deadlier than the original virus.

The new analysis relies on the database of Maccabi Healthcare Services, which enrolls about 2.5 million Israelis. The study, led by Tal Patalon and Sivan Gazit at KSM, the system's research and innovation arm, found in two analyses that never-infected people who were vaccinated in January and February were, in June, July, and the first half of August, six to 13 times more likely to get infected than unvaccinated people who were previously infected with the coronavirus. In one analysis, comparing more than 32,000 people in the health system, the risk of developing symptomatic COVID-19 was 27 times higher among the vaccinated, and the risk of hospitalization eight times higher.

"The differences are huge," says Thålin, although she cautions that the numbers for infections and other events analyzed for the comparisons were "small." For instance, the higher hospitalization rate in the 32,000-person analysis was based on just eight hospitalizations in a vaccinated group and one in a previously infected group. And the 13-fold increased risk of infection in the same analysis was based on just 238 infections in the vaccinated population, less than 1.5% of the more than 16,000 people, versus 19 reinfections among a similar number of people who once had SARS-CoV-2.

No one in the study who got a new SARS-CoV-2 infection died—which prevented a comparison of death rates but is a clear sign that vaccines still offer a formidable shield against serious disease, even if not as good as natural immunity. Moreover, natural immunity is far from perfect. Although reinfections with SARS-CoV-2 are rare, and often asymptomatic or mild, they can be severe.

In another analysis, the researchers compared more than 14,000 people who had a confirmed SARS-CoV-2 infection and were still unvaccinated with an equivalent number of previously infected people who received one dose of the Pfizer-BioNTech vaccine. The team found that the unvaccinated group was twice as likely to be reinfected as the singly vaccinated.

"We continue to underestimate the importance of natural infection immunity … especially when [infection] is recent," says Eric Topol, a physician-scientist at Scripps Research. "And when you bolster that with one dose of vaccine, you take it to levels you can't possibly match with any vaccine in the world right now."

Nussenzweig says the results in previously infected, vaccinated people confirm laboratory findings from a series of papers in *Nature* and *Immunity* by his group, his Rockefeller University colleague Paul Bieniasz and others—and from a preprint posted this month by Bieniasz and his team. They show, Nussenzweig says, that the immune systems of people who develop natural immunity to SARS-CoV-2 and then get vaccinated produce exceptionally broad and potent antibodies against the coronavirus. The preprint, for example, reported that people who were previously infected and then vaccinated with an mRNA vaccine had antibodies in their blood that neutralized the infectivity of another virus, harmless to humans, that was engineered to express a version of the coronavirus spike protein that contains 20 concerning mutations. Sera from vaccinated and naturally infected people could not do so.

As for the Israel medical records study, Topol and others point out several limitations, such as the inherent weakness of a retrospective analysis compared with a prospective study that regularly tests all participants as it tracks new infections, symptomatic infections, hospitalizations, and deaths going forward in time. “It will be important to see these findings replicated or refuted,” says Natalie Dean, a biostatistician at Emory University.

She adds: “The biggest limitation in the study is that testing [for SARS-CoV-2 infection] is still a voluntary thing—it’s not part of the study design.” That means, she says, that comparisons could be confounded if, for example, previously infected people who developed mild symptoms were less likely to get tested than vaccinated people, perhaps because they think they are immune.

Nussenzweig’s group has published data showing people who recover from a SARS-CoV-2 infection continue to develop increasing numbers and types of coronavirus-targeting antibodies for up to 1 year. By contrast, he says, twice-vaccinated people stop seeing increases “in the potency or breadth of the overall memory antibody compartment” a few months after their second dose.

For many infectious diseases, naturally acquired immunity is known to be more powerful than vaccine-induced immunity and it often lasts a lifetime. Other coronaviruses that cause the serious human diseases severe acute respiratory syndrome and Middle East respiratory syndrome trigger robust and persistent immune responses. At the same time, several other human coronaviruses, which usually cause little more than colds, are known to reinfect people regularly.

Clarification, 28 August, 1:20 p.m.: *This article has been updated to reflect that in an analysis involving previously infected people who received one vaccine dose, not all people received that dose after, rather than before, becoming infected. It has also been updated to clarify that the vaccinated people in the other two analyses had never been infected prior to being vaccinated.*

McKnights Long-Term Care News

NEWS

Health economists urge CMS to mandate COVID-19 staff vaccinations through quick rule-making process

KIMBERLY MARSELAS

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AUGUST 11, 2021

SHARE

A trio of prominent health policy experts is calling on the Centers for Medicare & Medicaid Services to "tap the levers" of its regulatory powers and use the Rules of Participation to require frontline nursing home workers to get vaccinated against the coronavirus.

"Unvaccinated healthcare workers put patients at high risk, given that their jobs require close interaction with unvaccinated patients and others who are immunocompromised and at higher risk for complications," wrote Jill Rosenthal, Emily Gee and Maura Calsyn of the Public Health Policy at the liberal-leaning Center for American Progress.

"Congregate settings, such as long-term care facilities, are particularly susceptible to the spread of infectious disease…. CMS should now update (the Rules of Participation) to mandate that healthcare and LTC staff and contractors, as well as healthcare providers with hospital privileges, are vaccinated against COVID-19."

The Rules of Participation govern the operations of all U.S. nursing homes receiving Medicaid or Medicare payments in exchange for caring for beneficiaries. Those that violate the rules are subject to penalties, and repeated infractions can lead to loss of certification and removal from the federal system.

To update such rules, CMS normally uses a notice-and-comment rulemaking process, but the authors noted the agency can instead adopt changes by issuing interim final rules when it finds there is "good cause" and the traditional process is "impracticable, unnecessary, or contrary to the public interest."

On Tuesday, the agency confirmed to *McKnight's Long-Term Care News* its authority to quickly institute workplace requirements in the name of patient safety, but officials did not say whether they are considering a vaccine mandate.

"The agency remains dedicated to ensuring nursing home staff and residents have the information they need to improve vaccination rates," a spokeswoman said, noting ongoing requirements to educate staff and residents about shots and report acceptance rates. "CMS has authority to establish requirements to ensure the health and safety of individuals receiving care from all providers and suppliers participating in the Medicare and Medicaid programs."

As proof of its willingness to advance change through its rule-making process, CMS cited the way it waived a notice-and-comment period when it added vaccine education and offering requirements to its rules governing skilled nursing providers in May.

In their paper, Rosenthal, director of Public Health Policy at the Center for American Progress, and colleagues argued that the emergence of the delta variant and stalled vaccination rates "have created the need for action beyond staff education and vaccine access."

"It is in the public interest to increase vaccination rates without delay, and mandatory vaccinations for healthcare workers are of critical importance in protecting patients' health and safety," they wrote. "CMS

should also evaluate whether it can impose civil monetary penalties, set to increase over time, for noncompliant organizations."

Other government officials are mandating

Several states in recent days have mandated vaccinations for nursing home workers, with Connecticut Gov. Ned Lamont (D) issuing an executive order that threatens operators with $20,000 per-day fines if their employees do not get vaccinated.

Likewise, federal and state agencies have begun to mandate vaccines for their own workers.

And officials in President Joe Biden's administration are also reportedly studying whether they can withhold Medicare funding from facilities with low staff vaccinations rates. But CMS issuing a vaccine mandate would remove non-compliant providers from their system, effectively shutting down access to much needed patients and the dollars that follow them.

Caslyn, Gee and Rosenthal developed their insights about rule-making authority over long careers in government or with non-governmental organizations. Caslyn is a former Department of Health and Human Services attorney who was responsible for several Medicare programs. Gee was on staff with the Council for Economic Advisers during the Obama administration. Rosenthal previously spent more than 20 years with the National Academy for State Health Policy.

They cited precedence for their call to force nursing homes into action through an ROP change: In 1965, federal officials required hospitals to desegregate to be eligible for Medicare reimbursement. More than 1,000 reluctant hospitals then integrated their staffs and hospital floors in less than four months.

"Importantly, (Rules of Participation) are national in scope, making them a powerful tool to effectuate change when there is local or regional reluctance," the authors wrote. "In areas with low vaccination rates, employers — including healthcare and LTC employers — may be less likely to adopt mandates on their own. State and local officials who have been resistant to public health measures such as masking are unlikely ever to adopt vaccine requirements for all workers in healthcare…. A consistent, national policy is necessary to overcome employers' perceived financial disincentive to mandate vaccination."

For its part, CMS said it "continues to analyze vaccination data for residents and staff from the CDC's NHSN data." That information, required to be reported weekly by all Medicare and Medicaid certified providers, showed 59.3% of nursing home staff were vaccinated per data submitted by July 25.

Trends that emerge among individual nursing homes or regionally inform how federal officials can deploy additional vaccines or other resources, such as Quality Improvement Organizations, to assist nursing homes

in encouraging vaccine uptake.

COVID-19 VACCINATION

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Contributors: SH and MW conceived the study. RH and JR provided scientific and technical oversight. AB designed and coded the data extraction, transformation and linkage. SC, AB, JS, ST, ON, and SG performed additional data processing and analyses. AB and SC drafted the paper. All authors provided input into to the interpretation of the results, contributed to revising the manuscript and approved the final version. AB and SC had full access to all the data in the study and final responsibility for the decision to submit for publication.

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Abstract

Objectives: Nosocomial transmission was an important aspect of SARS-CoV-1 and MERS-CoV outbreaks. Healthcare-associated SARS-CoV-2 infection has been reported in single and multi-site hospital-based studies in England, but not nationally.

Methods: Admission records for all hospitals in England were linked to SARS-CoV-2 national test data for the period 01/03/2020 to 31/08/2020. Case definitions were: community-onset community-acquired (CO.CA), first positive test (FPT) <14 days pre-admission, up to day 2 of admission; hospital-onset indeterminate healthcare-associated (HO.iHA), FPT on day 3-7; hospital-onset probable healthcare-associated (HO.pHA), FPT on day 8-14; hospital-onset definite healthcare-associated (HO.HA), FPT from day 15 of admission until discharge; community-onset possible healthcare-associated (CO.pHA), FPT ≤14 days post-discharge.

Results: One-third (34.4%, 100,859/293,204) of all laboratory-confirmed COVID-19 cases were linked to a hospital record. HO.pHA and HO.HA cases represented 5.3% (15,564/293,204) of all laboratory-confirmed cases and 15.4% (15,564/100,859) of laboratory-confirmed cases among hospital patients. CO.CA and CO.pHA cases represented 86.5% (253,582/293,204) and 5.1% (14,913/293,204) of all laboratory-confirmed cases, respectively.

Conclusions: Up to 1 in 6 SARS-CoV-2 infections among hospitalised patients with COVID-19 in England during the first 6 months of the pandemic could be attributed to nosocomial transmission, but these represent less than 1% of the estimated 3 million COVID-19 cases in this period.

Keywords: SARS-CoV-2; COVID-19; healthcare-associated infection; community-onset infection

Introduction

Healthcare-associated (nosocomial) transmission was a salient feature of SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) outbreaks, with 24% of SARS-CoV-1 infections and 36% of MERS-CoV infections among hospitalised cases (excluding healthcare workers) attributed to healthcare acquisition.[1] Early in the COVID-19 pandemic, a single-centre study in Wuhan, China, reported that 57 (41%) of 138 COVID-19 cases were nosocomial, of whom 17 were patients already hospitalised for other reasons and 40 were healthcare workers.[2] High rates of SARS-CoV-2 nosocomial infection among patient-facing healthcare workers and resident-facing social care workers were subsequently reported, in England representing 10% of all COVID-19 cases from 26th April to 7th June 2020.[3]

In the UK, a multi-site study of healthcare-associated COVID-19 during the first two months of the pandemic indicated that 13% of SARS-CoV-2 infections in hospital patients might be nosocomial,[4] whilst a London hospital reported 15% of COVID-19 cases being hospital-acquired during the same period.[5] In the context of rapidly increasing case numbers in most European countries during a second phase of the COVID-19 pandemic, and a paucity of available national data from almost all countries, there is a need to quantify healthcare-associated SARS-CoV-2 infection in hospitals. We calculated numbers of community-onset and hospital-onset healthcare-associated laboratory-confirmed COVID-19 cases in England during the first six months of the pandemic by linking national routinely collected data for SARS-CoV-2 test results with hospital admission data.

Methods

Data sources and linkage

Public Health England (PHE) collects data on all SARS-CoV-2 (COVID-19) PCR tests from laboratories across England.[6] Laboratory data systems feed automatically into PHE's Second Generation Surveillance System (SGSS).[7] In SGSS, the date the test sample was taken is recorded

as the 'specimen date'. We used this date in our analysis for positive SARS-CoV-2 tests, referred to throughout this paper as the 'test date'. In cases with multiple SARS-CoV-2 positive tests, the earliest positive test date was retained.

Data on all hospital attendances and admissions in England are collated by NHS Digital and sent daily to PHE via the Secondary Uses Service (SUS) and Emergency Care Dataset (ECDS) data collections for admitted patient stays and Accident and Emergency (A&E) attendances, respectively. SUS data are reported monthly, ECDS daily, both on a mandatory schedule.

SUS data are presented in consultant episodes, where a patient is under the continuous care of a single consultant.[8] Episodes were grouped into spells, with a continuous inpatient (CIP) spell comprising one or more consultant episodes within a single hospital provider. The standard NHS Digital methodology for creating CIPs was adapted to restrict hospital spells to a single provider.[9] When CIPs overlapped in time within a single provider, they were joined. Hospital records from ECDS and SUS were joined into a single continuous record of patient stay when an A&E attendance ended with a discharge coded as an inpatient admission to the same hospital provider for the same patient. Charlson comorbidity indices were calculated from ICD-10 codes for a spell using the method of Quan *et al.* and grouped as 0, 1 or ≥2 comorbidities.[10]

Mortality data were obtained from the PHE National Incident Coordination Centre (NICC) Epidemiology Cell (EpiCell). These data are derived from four sources: deaths notified by hospitals to NHS England; deaths notified to local PHE Health Protection Teams; laboratory reports where a laboratory-confirmed test result has been linked to a hospital-recorded death; and UK Office for National Statistics (ONS) death registrations.[11] A COVID-19 death was defined as a death that occurred ≤28 days after the first positive SARS-CoV-2 test.

Hospital records from ECDS and/or SUS were linked to SGSS COVID-19 positive test records deterministically using patient NHS number and date of birth else local hospital patient identifier (hospital number) and date of birth. SUS, ECDS and SGSS extracts were obtained on 09/12/2020,

mortality data on 14/10/2020. The study period was bounded by first positive test dates between 01/03/2020 and 31/08/2020.

Community-onset and hospital-onset classifications

Allocation to a community-onset or hospital-onset category was determined using the first positive SARS-CoV-2 test result paired with hospital record start date (emergency care attendance date or inpatient date of admission, where date of admission is day 1) or end date (inpatient date of discharge) according to the following classifications (illustrated by examples in Figure 1):[12]

- Community-onset community-acquired (CO.CA): positive test date <14 days pre-admission/attendance and up to day 2 of admission; no prior discharge within 14 days of admission/attendance
- Community-onset possible healthcare-associated (CO.pHA): positive test date ≤14 days post-discharge; if readmitted during this period, up to day 2 of admission where date of readmission is day 1
- Hospital-onset indeterminate healthcare-associated (HO.iHA): positive test from day 3 to day 7 of admission, inclusively
- Hospital-onset probable healthcare-associated (HO.pHA): positive test from day 8 to day 14 of admission, inclusively
- Hospital-onset definite healthcare-associated (HO.HA): positive test from day 15 of admission until day of discharge, inclusively
- Unclassified: All cases which do not meet one of the above criteria, i.e., the positive test did not have a relevant temporal link to a hospital admission or A&E attendance

For each positive test, a single hospital admission was retained for the final onset categorisation. When a patient had multiple hospital admissions, prioritisation was given to an admission overlapping with a positive sample date; when admissions conflicted on the same day in two different trusts, SUS took priority over ECDS data; when a patient had a positive sample between

two hospital stays, the completed hospital stay following the positive test was used unless the time between the discharge and positive test was greater than 14 days in which case the admission prior to the test was used. When the only evidence of an admission was an A&E discharge coded as an admission or transfer, the patient was assumed to be still in hospital at the time of data extraction, up to a maximum of 90 days between admission and positive test result, after which, the temporal link is discarded, and the specimen is considered unlinked.

Analyses of community- and hospital-onset COVID-19 excluded SARS-CoV-2 positive cases who had no ECDS or SUS record meeting the temporal criteria for community- or hospital-onset infection (or no ECDS or SUS record) or which were missing both NHS and hospital numbers, except when the denominator for analysis was all reported SARS-CoV-2 positive cases, for which ‘unlinked’ cases were classified as CO.CA.

Length of stay was calculated as the total time (in days) between attendance and discharge, starting with overnight bed-days in A&E, if applicable, or an inpatient admission. For hospital-onset cases, post-test length of stay was calculated as the time (in days) between the first positive test date and the date of discharge. Length of stay for CO.pHA cases are classified as 0 unless the case definition for both CO.pHA and CO.CA are met for the inpatient stay.

Statistical analyses were descriptive, comprising frequencies and percentages for community-onset and hospital-onset classifications stratified by month, region, and provider type (and, for NHS acute and mental health and learning disability trusts, by age group, sex, ethnicity, and Charlson score) and mortality, and median with interquartile range (IQR) for age and length of hospital stay.

Ethics: All data were collected within statutory approvals granted to Public Health England for infectious disease surveillance and control. Information was held securely and in accordance with the Data Protection Act 2018 and Caldicott guidelines.

Role of the funding source: The funders had no role in the design, data collection, analysis or manuscript preparation.

Results

Community-onset and hospital-onset COVID-19 cases in England, March-August

Of the 293,204 laboratory-confirmed COVID-19 cases in England with a first positive SARS-CoV-2 test date between March 1st and August 31st, 2020, 100,859 (34.4%) were linked to a time-relevant emergency care attendance and/or hospital admission, 167,467 (57.1%) had no time-relevant hospital record and 24,878 (8.5%) had missing NHS and hospital numbers. The proportion of all laboratory-confirmed cases linked to a hospital record declined from a maximum of 79.2% (25,874/32,682) in March to 6.9% (2,054/29,807) in August (Figure S1).

Probable and definite (HO.pHA and HO.HA) hospital-onset healthcare-associated cases represented 5.3% (15,564/293,204) of all laboratory-confirmed COVID-19 cases and 15.4% (15,564/100,859) of cases among hospital patients in England (**Table 1**). Community-onset cases (CO.CA and CO.pHA) represented 91.6% (268,495/293,204) of all laboratory-confirmed cases and 75.5% (76,150/100,859) of laboratory-confirmed cases with a hospital admission; of the latter, 19.6% (14,913/76,150) were possibly healthcare-associated, representing 5.1% of all laboratory-confirmed COVID-19 cases.

As monthly proportions of hospital patients with COVID-19, HO.pHA and HO.HA hospital-onset healthcare-associated cases peaked during May and June, at 21.0% (3,122/14,905) and 21.9% (1,223/5,590), respectively (**Figure 2, Figure 3**). The peak in HO.pHA and HO.HA cases occurred in week 22 (27th May to 2nd June) at 26.5% (558/2,109), double the proportion in week 14 (1st to 7th April) at 12.7% (2,342/18,687), which was the week with highest number of laboratory-confirmed cases linked to a hospital record (18,687 linked cases, from a total of 27,671 laboratory-confirmed cases).

There was considerable variation across regions of England in the proportions of hospital patients classified as HO.pHA and HO.HA, from 11.2% (2,427/21,770) in London to 19.3% (3,173/16,427) in the North West NHS region (**Table 2**). A higher proportion of laboratory-confirmed cases linked to Mental Health and Learning Disability NHS Trusts were classified as probable or definite healthcare-associated (54.2%, 1,253/2,310) compared with NHS Acute Trusts (14.3%, 13,875/97,372) (**Table 3**).

Characteristics and outcomes of community-onset and hospital-onset COVID-19 cases

The median (IQR) age of hospital patients with a positive test in NHS Acute Trusts was 71 (54-83) years compared with 77 (62-85) years for NHS Mental Health and Learning Disability Trusts. Among NHS Acute Trust hospital patients who tested positive for SARS-CoV-2, older patients (age ≥60 years) were more likely to have a hospital-onset probable or definite healthcare-associated infection (18.5% (12,106/65,534)) than patients under 60 years of age (5.6% (1,769/31,830)) (**Table 4, Figure 4**). Among NHS Mental Health and Learning Disability Trust patients, 55.9% (989/1,769) of laboratory-confirmed COVID-19 cases in patients aged 60 years and older were hospital-onset probable or definite healthcare-associated compared with 48.8% (264/541) of laboratory-confirmed cases in patients under 60 years of age (**Table S1**).

Among patients in Acute Trusts, HO.HA cases had the longest total length of stay (median 41, IQR 28-72 days) and longest post-test length of stay (median 13, IQR 6-27 days (**Table 4**). In Mental Health and Learning Disability Trusts, the median total length of stay for HO.HA cases was 83 days (IQR 44-231 days); the median post-test length of stay for these cases was 29 (IQR 12-79) days (**Table S1**).

The proportions of patients with 2 or more comorbidities (Charlson index ≥2) in NHS Acute Trust ranged from 42% in CO.CA cases to 70% in HO.HA cases (**Table 4**). HO.pHA and HO.HA patients in NHS Acute Trusts had 41.3% (5,726/13,875) 28-day COVID-related mortality, compared with 25.9% (15,620/60,233) in CO.CA cases (**Table 4, Table S2**). In patients in NHS

Mental Health and Learning Disability Trusts, 28-day mortality among HO.pHA and HO.HA cases was 21.9% (274/1,253) (**Table S1**).

Discussion

Our study of healthcare-associated COVID-19 in hospital patients, encompassing the first phase of the COVID-19 pandemic in England, is the first to use large-scale national data. We found that 15% of patients admitted with or diagnosed during admission with SARS-CoV-2 infection during the first 6 months of the pandemic were hospital-onset probable or definite healthcare-associated, representing 5% of all laboratory-confirmed COVID-19 cases during this period. A further 15% of laboratory-confirmed cases in hospital patients who had COVID-19 were possibly healthcare-associated but with a first positive test after discharge.

Our results are descriptive. We did not attempt more in-depth analyses, our aim being to present an overall picture of healthcare-associated COVID-19. Further analyses of national data might be useful, although the time-varying nature of many of the factors involved in COVID-19, particularly testing practices, and fundamental differences between community and hospital populations and between hospitals may preclude a meaningful analysis of such observational data. Instead, smaller prospective studies with well-characterized patient cohorts and complete epidemiological data may be more useful in determining risk factors for healthcare-associated SARS-CoV-2 infection and providing evidence to inform infection prevention and control measures in healthcare settings.

In the context of other studies and reports

Our estimated proportion for HO.pHA and HO.HA combined was consistent with other reports: a study in 10 UK hospitals and 1 Italian hospital reported 13% up to 28th April,[4] and a single London hospital reported 15% between 2nd March and 12th April.[5] Although our data covered the period up to 30th August, 75% of laboratory-confirmed cases linked to hospital records occurred during March and April, and the HO.pHA and HO.HA proportion in our dataset for those two months (14%) was

only slightly lower than our estimate for the whole 6-month period. Hospital-onset cases to 30th August represented 6.4% of all laboratory-confirmed COVID-19 cases in Scotland and 10.5% of all laboratory-confirmed COVID-19 cases in Wales.[13,14] The lower proportion (5.3%) in England may reflect differences in hospital admissions or testing over the peak months.

There is a growing international literature on nosocomial SARS-CoV-2 infection, from single ward or department reports,[15-23] to hospital-wide studies,[24-26] but only one (from Malta) based on limited national surveillance data.[27] The lull between phases of the pandemic in Europe has allowed prospective studies to be planned, but these have yet to report.[28] Early estimates for nosocomial COVID-19 will be highly variable because responses to the pandemic changed rapidly over time, most notably in SARS-CoV-2 testing in the community and in healthcare settings.

The 28-day mortality rate (26%) for community-onset community-acquired cases admitted to NHS Acute hospitals in our study was consistent with in-hospital mortality reported directly by NHS Acute hospitals (26%).[29] Hospital-onset cases experienced higher mortality, as expected given their higher median age (79 years for HO.HA cases compared with 66 years for CO.CA cases) and pre-existing conditions. The higher proportion of hospital-onset cases in Mental Health and Learning Disability Trusts probably reflects longer stays in these settings, which include residential and secure psychiatric units, compared with Acute Trusts; COVID-19 mortality among hospital-onset cases in Mental Health and Learning Disability Trust patients (22% for HO.pHA and HO.HA) was lower than in community-onset cases in acute hospitals. However, as noted above, these crude comparisons do not consider a multiplicity of differences between patient groups. Mental health hospitals had relatively fewer inpatients with COVID-19, therefore nosocomial proportions are based on much smaller denominators. It is also possible that case detection may have been sub-optimal in such settings.

Strengths and limitations

The strength of our study is that centralised, routinely collected national data sources were used which recorded all positive COVID-19 test results from Pillars 1 and 2 of the UK government's public testing programmes, and all NHS hospital attendances and admissions in England. The latter represented approximately 98% of all hospital activity in the country.[30] Pillar 1 tests were provided by NHS and PHE laboratories for community cases from January 16th to March 12th, 2020, for hospitalised cases and the investigation of care home outbreaks from March 12th to March 31st, 2020, and for healthcare workers and their families from April 1st onwards (where additional capacity was available). Pillar 2 testing was delivered by central government through academic, public and private partnerships: from April 1st 2020 it was progressively rolled out to key workers in the NHS, social care and other critical sectors; from May 23rd the general population could also access testing from this route; from August 1st it was used to test asymptomatic staff and residents in care homes and for asymptomatic contacts in outbreak investigations. We saw a large expected decrease in the proportion of cases with a temporal link to a hospital record (from 79% in March to 7% in August), as testing policy across the UK expanded from an initial focus on testing in hospitals to community testing.

The main limitation of our study is that our case numbers reflect national testing activity, not the true number of cases in the population, and this activity was severely constrained by testing capacity during the phase of the pandemic covered by our study. As of September 8th, 2020, it was estimated from household survey data that approximately 2.8 million people (95% CI 2.4 to 3.2 million people) aged 16 years and over would have antibodies to COVID-19.[31] Therefore, the 15,564 HO.pHA and HO.HA cases during this six-month period represent approximately 1% of all cases in England at the time of this estimate. While numbers of hospital-onset cases should be closer to the true number of cases, assuming that patients in hospital were more likely to be tested, an unknown number of asymptomatic cases will have been missed where inpatients were not routinely swabbed. Systematic testing of inpatients in hospitals in England did not start until 24th

June. Similarly, cases classified as probable or definite hospital-onset may have been infected before admission or during the first 7 days of admission but were not tested until they became symptomatic, or they may have had negative test results, which were not available for our analysis. The overall effect of these limitations will likely have been to over-estimate probable and definite hospital-onset case numbers. Linkage of national surveillance and hospital activity data will be imperfect, and our algorithm made assumptions in assigning a priority order when test result data linked to more than one attendance or admission. For CO.pHA cases, we treated all hospital admissions equally regardless of duration of healthcare exposure. Conversely, we would not have captured infections potentially acquired from primary care, outpatient and emergency department attendances. Our data did not allow us to identify healthcare workers whose infection may have been acquired in the workplace, and we would have misclassified these cases as community-acquired. Our analysis used test and admission dates rather than dates and times because time of day was not recorded in our test or inpatient data sources, therefore our results will not be exactly comparable with classifications based on exact time, i.e., ≤48 hours rather than ≤2 days.

Implications for policy and practice

Frontline healthcare workers were identified as a high-risk group during the first phase of the pandemic,[32] highlighting an urgent need for personal protective equipment and procedures. This was of particular importance to protect staff for their own safety, to prevent onward transmission to patients, to minimise staff absence at a time of extraordinarily high demand on the NHS.[33] andbecause patients may be in an incubation period or have a false negative test.[24] Arguably, countries which had direct experience of SARS-CoV-1 were better prepared to respond to the risk of healthcare-associated COVID-19.[25] In countries such as the UK, which are experiencing distinct phases of the pandemic, preparedness for subsequent phases should be better than during the first phase, including the availability of comprehensive guidelines for infection prevention and control in different healthcare settings and for care of patients at increased risk of severe COVID-19 illness.[34]

To reduce transmission in hospitals from patient to patient and from patient to healthcare worker, the UK now recommends pre-admission testing of all patients who are to be admitted for elective procedures, testing on admission for emergency admissions, and testing at 3-7 days post-admission. To reduce transmission of asymptomatic or pre-symptomatic COVID-19 from healthcare worker to healthcare worker and from healthcare worker to patient, hospitals are recommended to screen staff on a weekly basis in periods of higher community prevalence, during hospital outbreaks and when cases of nosocomial COVID-19 are detected. More extensive (3 times a week) screening of patient facing healthcare workers in the NHS has recently been rolled out.

Currently, very limited rapid emergency care testing will likely have two main consequences for nosocomial infection: firstly, within A&E, because positive and negative patients cannot be readily identified in a setting of crowded units and waiting areas; secondly, patients with unknown COVID-19 status are admitted to a hospital bed, typically in 4-, 6- or 10-bedded bays. Lastly, and crucially, the proportion of NHS hospital beds in England that are in single rooms is approximately 20%, which severely constrains capacity to prevent airborne virus transmission.

Figure legends

Figure 1: Examples illustrating classification of patients admitted to hospitals in England who tested positive for SARS-CoV-2 as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA), and community-onset possible healthcare-associated (CO.pHA)

Figure 2: Patients admitted to hospitals in England who tested positive for SARS-CoV-2, showing the weekly numbers of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA), and community-onset possible healthcare-associated (CO.pHA)

Figure 3: Patients admitted to hospitals in England who tested positive for SARS-CoV-2, showing the weekly proportions of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA), and community-onset possible healthcare-associated (CO.pHA)

Figure 4: Patients admitted to NHS Acute Trust hospitals in England who tested positive for SARS-CoV-2, showing the proportions of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA), and community-onset possible healthcare-associated (CO.pHA) by age group.

Figure S1: Patients admitted to hospitals in England who tested positive for SARS-CoV-2, showing the weekly numbers of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA) and community-onset possible healthcare-associated (CO.pHA) and laboratory-confirmed COVID-19 cases not linked to a hospital admission (Unlinked)

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Table 1: Monthly community-onset and hospital-onset COVID-19 as proportions of all laboratory-confirmed COVID-19 cases and as proportions of all hospital patients who tested positive for SARS-CoV-2

			Community-onset community-acquired†	Hospital-onset indeterminate healthcare-associated	Hospital-onset probable healthcare-associated	Hospital-onset definite healthcare-associated	Community-onset possible healthcare-associated
March	Positive for SARS-CoV-2			n=2,583	n=1,397	n=2,643	n=3,380
	as % of all laboratory-confirmed COVID-19 cases	(N=32,682)	69.4% (n=22,679)	7.9%	4.3%	8.1%	10.3%
	as % of hospital patients with COVID-19	(N=25,874)	61.3% (n=15,871)	10.0%	5.4%	10.2%	13.1%
April	Positive for SARS-CoV-2			n=4,570	n=3,036	n=3,627	n=7,216
	as % of all laboratory-confirmed COVID-19 cases	(N=117,915)	84.4% (n=99,466)	3.9%	2.6%	3.1%	6.1%
	as % of hospital patients with COVID-19	(N=50,119)	63.2% (n=31,670)	9.1%	6.1%	7.2%	14.4%
May	Positive for SARS-CoV-2			n=1,254	n=1,667	n=1,455	n=2,700
	as % of all laboratory-confirmed COVID-19 cases	(N=67,967)	89.6% (n=60,891)	1.9%	2.5%	2.1%	4.0%
	as % of hospital patients with COVID-19	(N=14,905)	52.5% (n=7,829)	8.4%	11.2%	9.8%	18.1%
June	Positive for SARS-CoV-2			n=449	n=597	n=626	n=1,035
	as % of all laboratory-confirmed COVID-19 cases	(N=25,496)	89.4% (n=22,789)	1.8%	2.3%	2.5%	4.1%
	as % of hospital patients with COVID-19	(N=5,590)	51.6% (n=2,883)	8.0%	10.7%	11.2%	18.5%
July	Positive for SARS-CoV-2			n=187	n=179	n=190	n=336
	as % of all laboratory-confirmed COVID-19 cases	(N=19,337)	95.4% (n=18,445)	1.0%	0.9%	1.0%	1.7%
	as % of hospital patients with COVID-19	(N=2,317)	61.5% (n=1,425)	8.1%	7.7%	8.2%	14.5%
August	Positive for SARS-CoV-2			n=102	n=64	n=83	n=246
	as % of all laboratory-confirmed COVID-19 cases	(N=29,807)	98.3% (n=29,312)	0.3%	0.2%	0.3%	0.8%
	as % of hospital patients with COVID-19	(N=2,054)	75.9% (n=1,559)	5.0%	3.1%	4.0%	12.0%
Overall				n=9,145	n=6,940	n=8,624	n=14,913
	as % of all laboratory-confirmed COVID-19 cases	(N=293,204)	86.5% (n=253,582)	3.1%	2.4%	2.9%	5.1%
	as % of hospital patients with COVID-19	(N=100,859)	60.7% (n=61,237)	9.1%	6.9%	8.6%	14.8%

† Denominator = all laboratory-confirmed cases, community-onset includes all COVID-19 cases not linked to a hospital record; denominator = hospital patients, community-onset excludes patients not linked to a hospital record

Table 2: Community-onset and hospital-onset COVID-19 as proportions of all hospital patients who tested positive for SARS-CoV-2 by NHS region

NHS region	Hospital patients positive for SARS-CoV-2	Community-onset community-acquired	Hospital-onset indeterminate healthcare-associated	Hospital-onset probable healthcare-associated	Hospital-onset definite healthcare-associated	Community-onset possible healthcare-associated
London	21,770	14,296 (65.7%)	2,089 (9.6%)	956 (4.4%)	1,471 (6.8%)	2,958 (13.6%)
Midlands	19,021	11,098 (58.4%)	1,823 (9.6%)	1,509 (7.9%)	1,652 (8.7%)	2,939 (15.5%)
North West	16,427	9,279 (56.5%)	1,397 (8.5%)	1,380 (8.4%)	1,793 (10.9%)	2,578 (15.7%)
North East & Yorkshire	15,208	9,581 (63.0%)	1,182 (7.8%)	920 (6.1%)	1,139 (7.5%)	2,386 (15.7%)
South East	12,873	7,659 (59.5%)	1,153 (9.0%)	1,040 (8.1%)	1,247 (9.7%)	1,774 (13.8%)
East of England	10,738	6,391 (59.5%)	1,115 (10.4%)	785 (7.3%)	797 (7.4%)	1,650 (15.4%)
South West	4,817	2,928 (60.8%)	386 (8.0%)	350 (7.3%)	525 (10.9%)	628 (13.0%)
Overall	100,854[†]	61,232 (60.7%)	9,145 (9.1%)	6,940 (6.9%)	8,624 (8.6%)	14,913 (14.8%)

[†] NHS region was not recorded for 5 CO.CA cases

Table 3: Community-onset and hospital-onset COVID-19 as proportions of all hospital patients who tested positive for SARS-CoV-2 by type of provider

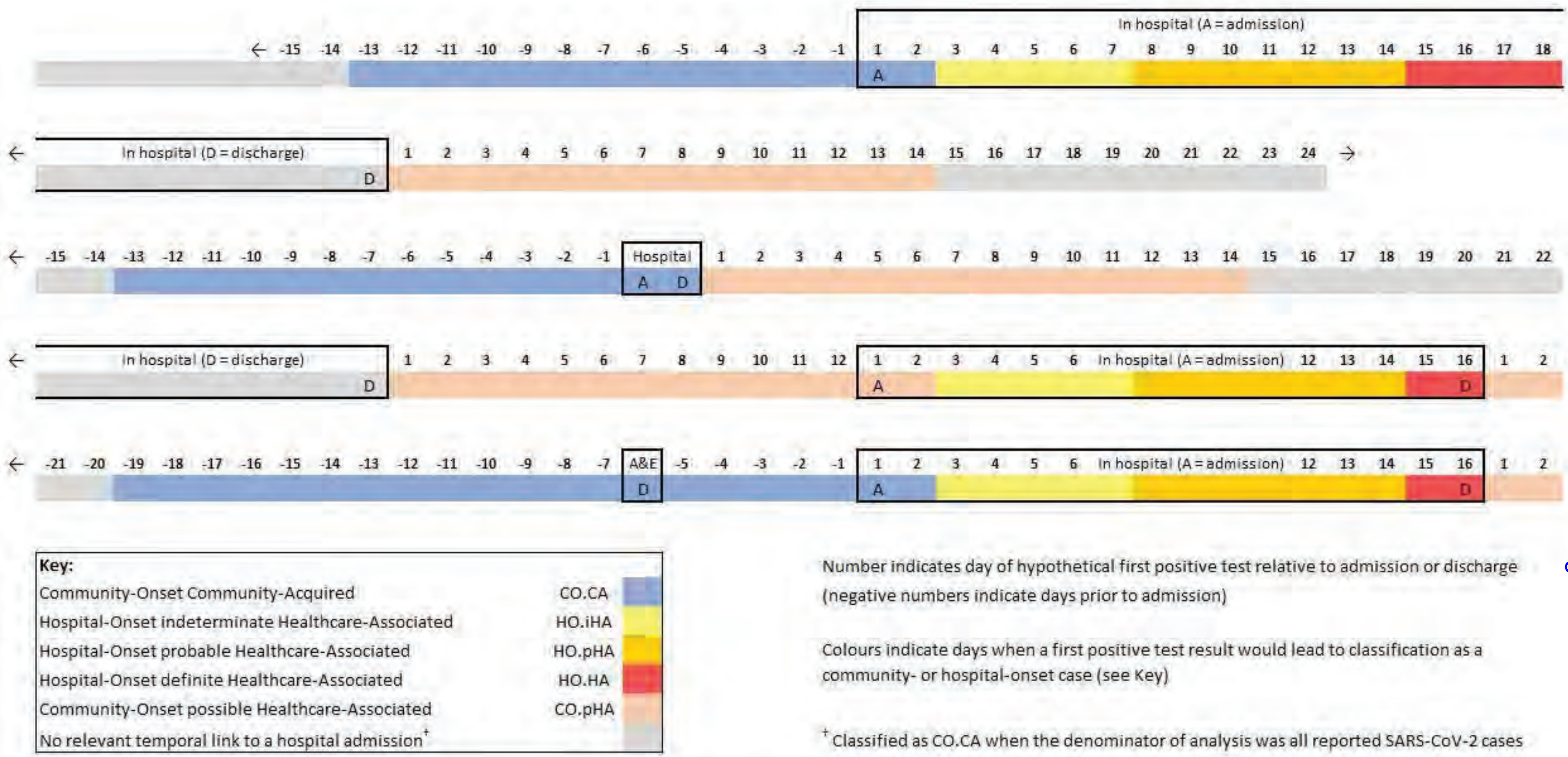
Healthcare provider	Hospital patients positive for SARS-CoV-2	Community-onset community-acquired	Hospital-onset indeterminate healthcare-associated	Hospital-onset probable healthcare-associated	Hospital-onset definite healthcare-associated	Community-onset possible healthcare-associated
NHS Acute Trust	97,372	60,233 (61.9%)	8,679 (8.9%)	6,435 (6.6%)	7,440 (7.6%)	14,585 (15.0%)
Independent (non-NHS providers)	490	303 (61.8%)	45 (9.2%)	48 (9.8%)	65 (13.3%)	29 (5.9%)
NHS Community Trust	663	157 (23.7%)	121 (18.3%)	136 (20.5%)	170 (25.6%)	79 (11.9%)
NHS Mental Health & Learning Disability Trust	2,310	539 (23.3%)	299 (12.9%)	320 (13.9%)	933 (40.4%)	219 (9.5%)
Overall	100,854[†]	61,232 (60.7%)	9,145 (9.1%)	6,940 (6.9%)	8,624 (8.6%)	14,913 (14.8%)

[†] Healthcare provider was not recorded for 5 CO.CA cases

Table 4: Characteristics and outcomes of community-onset and hospital-onset laboratory-confirmed COVID-19 cases in NHS Acute Trusts

		Hospital patients positive for SARS-CoV-2	Community-onset community-acquired	Hospital-onset indeterminate healthcare-associated	Hospital-onset probable healthcare-associated	Hospital-onset definite healthcare-associated	Community-onset possible healthcare-associated
		N=97,372	n=60,233	n=8,679	n=6,435	n=7,440	n=14,585
Age (years)	<18 years	1,305 (1.3%)	901 (1.5%)	81 (0.9%)	15 (0.2%)	66 (0.9%)	242 (1.7%)
	18-29 years	3,714 (3.8%)	2,957 (4.9%)	154 (1.8%)	41 (0.6%)	94 (1.3%)	468 (3.2%)
	30-39 years	5,769 (5.9%)	4,589 (7.6%)	282 (3.3%)	88 (1.4%)	108 (1.5%)	702 (4.8%)
	40-49 years	8,263 (8.5%)	6,415 (10.7%)	496 (5.7%)	179 (2.8%)	238 (3.2%)	935 (6.4%)
	50-59 years	12,779 (13.1%)	9,316 (15.5%)	975 (11.2%)	398 (6.2%)	542 (7.3%)	1,548 (10.6%)
	60-69 years	13,737 (14.1%)	8,775 (14.6%)	1,294 (14.9%)	731 (11.4%)	925 (12.4%)	2,012 (13.8%)
	70-79 years	19,151 (19.7%)	10,370 (17.2%)	1,964 (22.6%)	1,537 (23.9%)	1,797 (24.2%)	3,483 (23.9%)
	80+ years	32,646 (33.5%)	16,904 (28.1%)	3,433 (39.6%)	3,446 (53.6%)	3,670 (49.3%)	5,193 (35.6%)
Sex	Female	45,121 (46.4%)	28,106 (46.7%)	3,806 (43.9%)	3,050 (47.4%)	3,526 (47.4%)	6,633 (45.5%)
	Male	52,228 (53.6%)	32,104 (53.3%)	4,873 (56.1%)	3,385 (52.6%)	3,914 (52.6%)	7,952 (54.5%)
Ethnicity (BAME = black and ethnic minority)	White	75,370 (78.4%)	43,956 (74.2%)	7,071 (82.1%)	5,867 (91.7%)	6,664 (90.3%)	11,812 (81.7%)
	BAME	20,762 (21.6%)	15,325 (25.8%)	1,546 (17.9%)	529 (8.3%)	716 (9.7%)	2,646 (18.3%)
Charlson score (range 0-16)	0	21,552 (25.7%)	15,053 (31.4%)	1,880 (22.3%)	815 (13.1%)	790 (11.3%)	3,014 (21.3%)
	1	20,574 (24.6%)	13,002 (27.1%)	2,100 (24.9%)	1,217 (19.5%)	1,309 (18.7%)	2,946 (20.8%)
	2+	41,641 (49.7%)	19,913 (41.5%)	4,466 (52.9%)	4,199 (67.4%)	4,888 (70.0%)	8,175 (57.8%)
Length of stay (hospital spell)	median (IQR) days	-	5 (1-11)	11 (7-19)	19 (14-28)	41 (28-72)	6 (3-13)
Length of stay (post-test)	median (IQR) days	-	4 (1-10)	7 (3-15)	9 (4-18)	13 (6-27)	6 (3-13)
Mortality (28 days post-test)		29,073 (29.9%)	15,620 (25.9%)	3,003 (34.6%)	2,840 (44.1%)	2,886 (38.8%)	4,724 (32.4%)

Figure 1: Classification of patients admitted to hospitals in England who tested positive for SARS-CoV-2 as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA) and community-onset possible healthcare-associated (CO.pHA)



AR-01394

Figure 2: Patients admitted to hospitals in England who tested positive for SARS-CoV-2, showing the weekly numbers of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA) and community-onset possible healthcare-associated (CO.pHA)

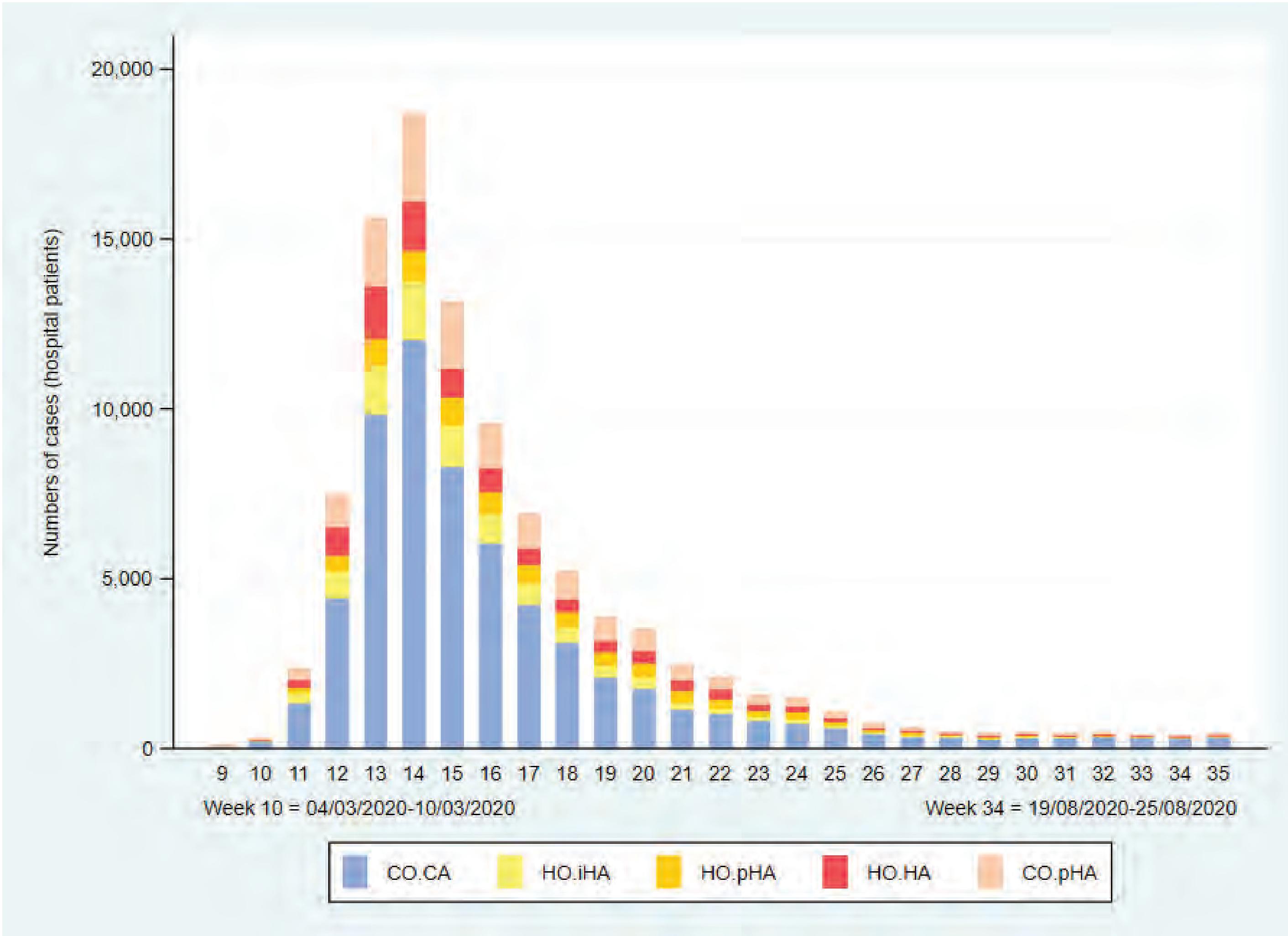
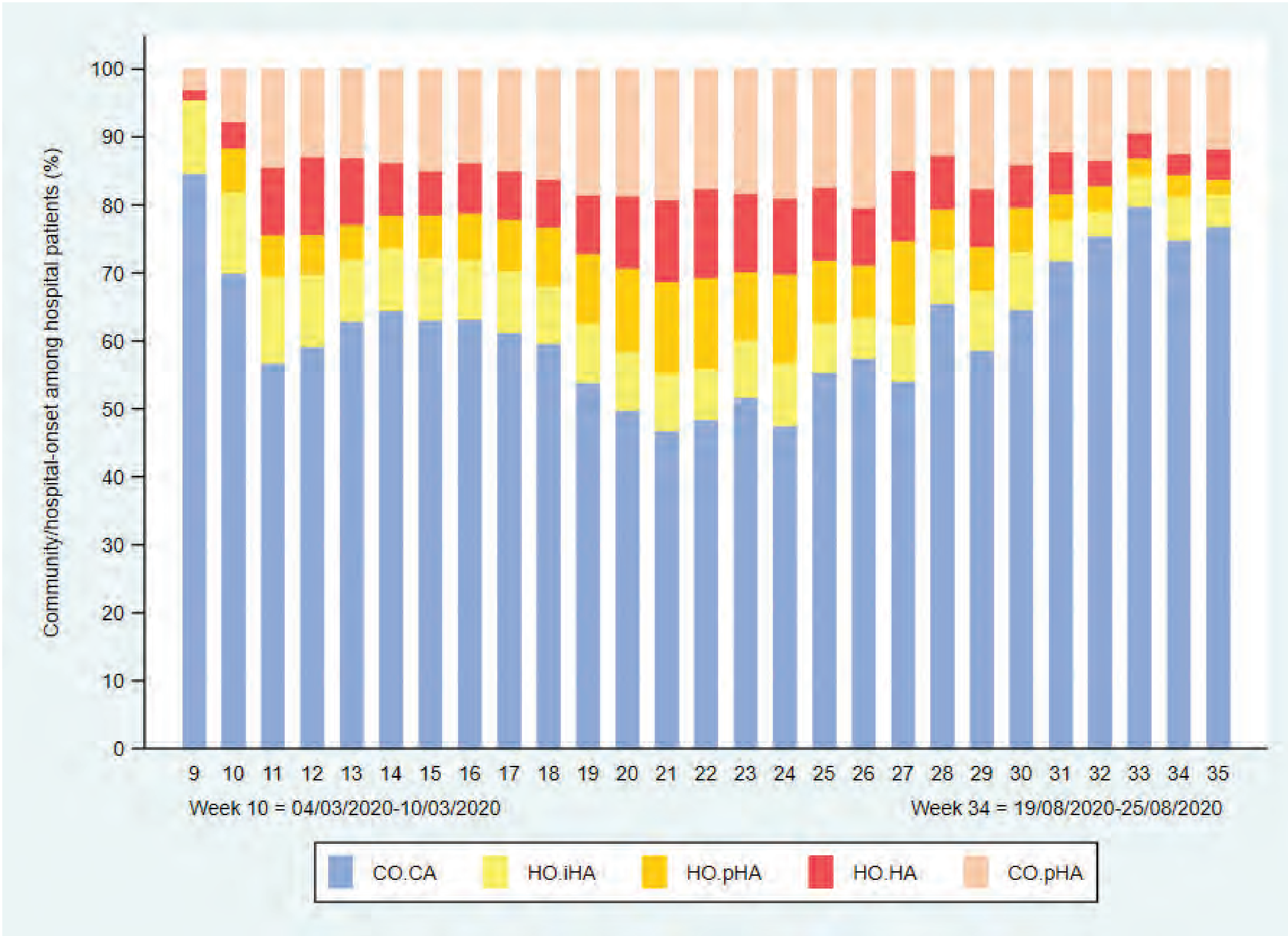


Figure 3: Patients admitted to hospitals in England who tested positive for SARS-CoV-2, showing the weekly percentages of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA) and community-onset possible healthcare-associated (CO.pHA)



AR-01396

Figure 4: Patients admitted to NHS Acute Trust hospitals in England who tested positive for SARS-CoV-2, showing the percentages of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA) and community-onset possible healthcare-associated (CO.pHA) by age group

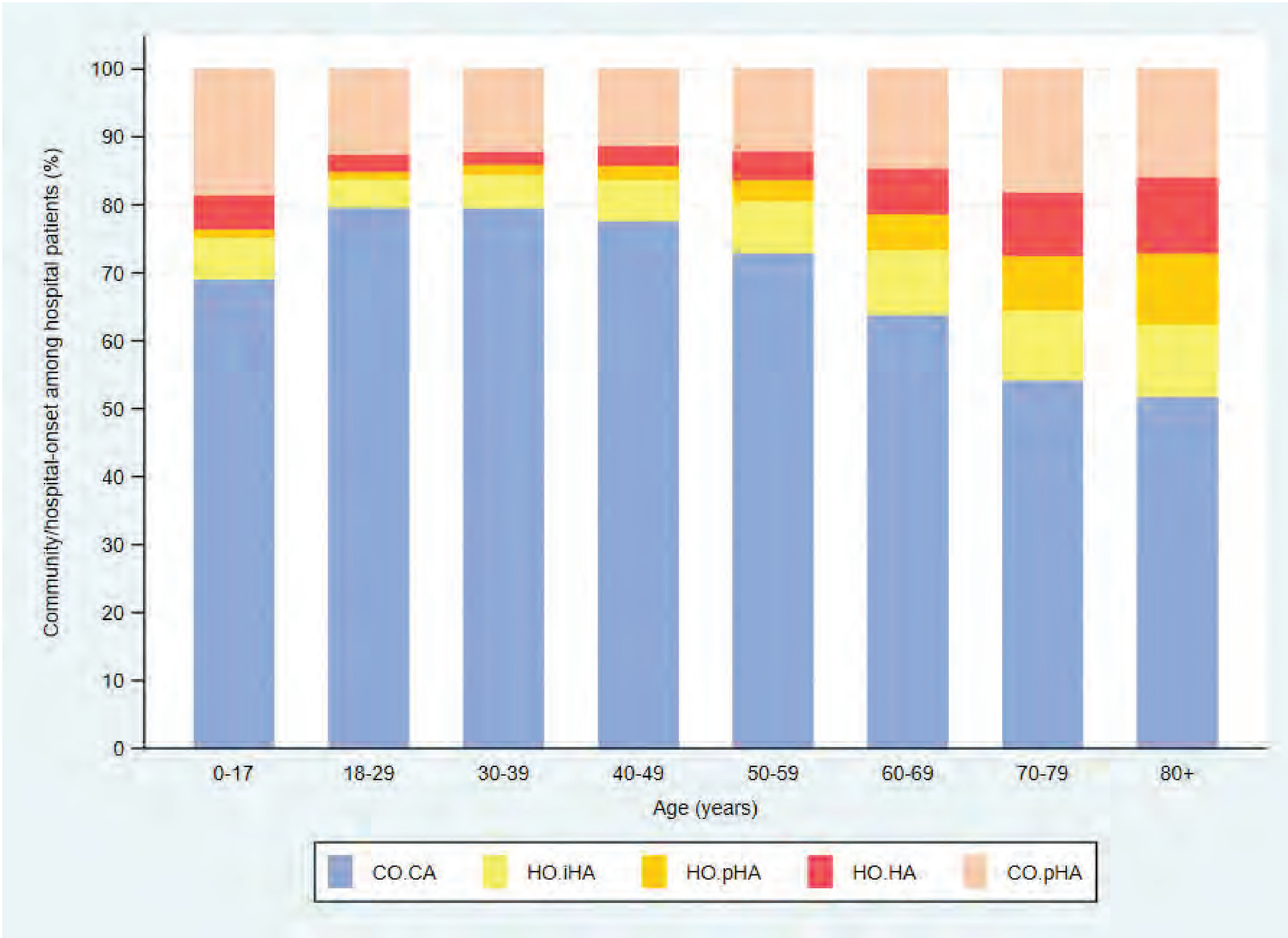
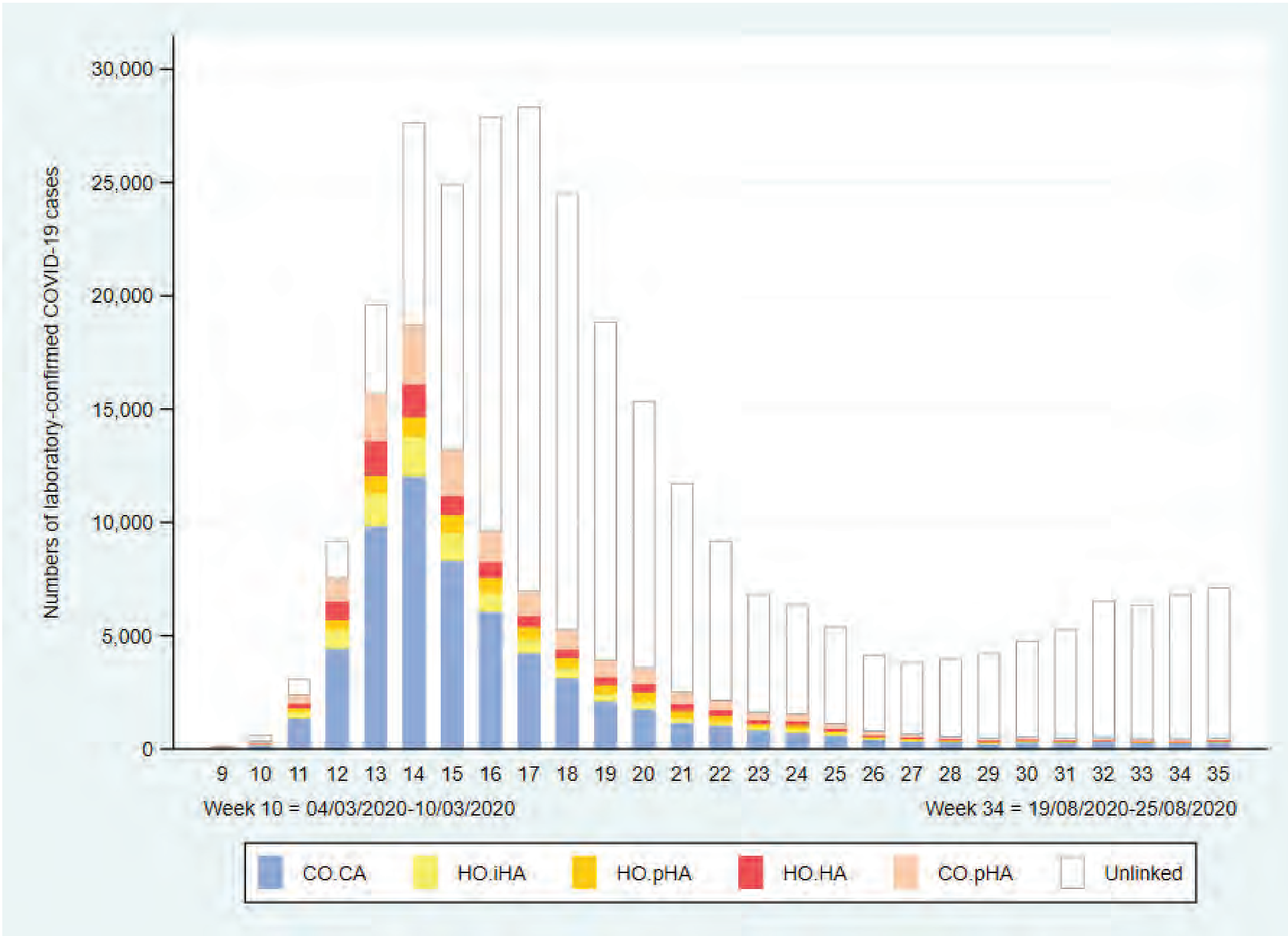


Figure S1: Patients admitted to hospitals in England who tested positive for SARS-CoV-2, showing the weekly numbers of cases classified as hospital-onset indeterminate, probable and definite healthcare-associated (HO.iHA, HO.pHA, HO.HA), community-onset community-acquired (CO.CA) and community-onset possible healthcare-associated (CO.pHA) and laboratory-confirmed COVID-19 cases not linked to a hospital admission (Unlinked)



AR-01398

Table S1: Characteristics and outcomes of community-onset and hospital-onset laboratory-confirmed COVID-19 cases in NHS Mental Health & Learning Disability Trusts (March to August 2020)

		Hospital patients positive for SARS-CoV-2	Community-onset community-acquired	Hospital-onset indeterminate healthcare-associated	Hospital-onset probable healthcare-associated	Hospital-onset definite healthcare-associated	Community-onset possible healthcare-associated
		N=2,310	n=539	n=199	n=320	n=933	n=219
Age (years)	0-39 years	229 (9.9%)	73 (13.5%)	21 (7.0%)	21 (6.6%)	99 (10.6%)	15 (6.9%)
	40-49 years	119 (5.2%)	48 (8.9%)	10 (3.3%)	14 (4.4%)	41 (4.4%)	6 (2.7%)
	50-59 years	193 (8.4%)	67 (12.4%)	20 (6.7%)	23 (7.2%)	66 (7.1%)	17 (7.8%)
	60-69 years	269 (11.7%)	69 (12.8%)	32 (10.7%)	31 (9.7%)	111 (11.9%)	26 (11.9%)
	70-79 years	530 (22.9%)	111 (20.6%)	63 (21.1%)	67 (20.9%)	244 (26.2%)	45 (20.6%)
	80+ years	970 (42.0%)	171 (31.7%)	153 (51.2%)	164 (51.3%)	372 (39.9%)	110 (50.2%)
Sex	Female	1,094 (47.4%)	255 (47.3%)	152 (50.8%)	146 (45.6%)	440 (47.2%)	101 (46.1%)
	Male	1,216 (52.6%)	284 (52.7%)	147 (49.2%)	174 (54.4%)	493 (52.8%)	118 (53.9%)
Ethnicity	White	2,121 (92.6%)	506 (96.0%)	276 (92.3%)	292 (91.8%)	835 (89.9%)	212 (97.3%)
	Black & ethnic minority	170 (7.4%)	21 (4.0%)	23 (7.7%)	26 (8.2%)	94 (10.1%)	6 (2.8%)
Charlson score (range 0-16)	0	918 (41.2%)	165 (35.6%)	146 (49.2%)	130 (40.6%)	409 (44.0%)	68 (31.1%)
	1	508 (22.8%)	121 (26.1%)	64 (21.6%)	67 (20.9%)	219 (23.6%)	37 (16.9%)
	2+	803 (36.0%)	177 (38.2%)	87 (29.3%)	123 (38.4%)	302 (32.5%)	114 (52.0%)
Length of stay (hospital spell)	median (IQR) days	-	5 (1-12)	18 (10-34)	27 (17-47)	83 (44-231)	9 (4-21)
Length of stay (post-test)	median (IQR) days	-	5 (1-12)	13 (5-28)	16 (6-34)	29 (12-79)	9 (4-21)
Mortality (28 days post-test)		518 (22.4%)	120 (22.4%)	75 (25.1%)	81 (25.3%)	193 (20.7%)	49 (22.4%)

Table S2: Mortality at 28 days (after first positive SARS-CoV-2 PCR test) by community- or hospital-onset COVID-19 case classification in patients admitted to NHS Acute Trust hospitals (March to August 2020)

CO.CA	age (years)	total	died (28d)	(%)
community-	0-39	3,858	42	1.1%
onset	40-49	6,415	276	4.3%
community-	50-59	9,316	946	10.2%
acquired	60-64	4,635	886	19.1%
	65-69	4,140	1,103	26.6%
	70-74	4,818	1,641	34.1%
	75-79	5,552	2,281	41.1%
	80-84	6,504	2,999	46.1%
	85-89	5,732	2,802	48.9%
	90+	4,668	2,565	54.9%
	Total	60,227	15,620	25.9%

CO.pHA	age (years)	total	died (28d)	(%)
community-	0-39	1,412	41	2.9%
onset	40-49	935	66	7.1%
possible	50-59	1,548	246	15.9%
healthcare-	60-64	934	210	22.5%
associated	65-69	1078	320	29.7%
	70-74	1,607	543	33.8%
	75-79	1,876	767	40.9%
	80-84	2,063	954	46.2%
	85-89	1878	932	49.6%
	90+	1252	645	51.5%
	Total	14,583	4,724	32.4%

HO.iHA	age (years)	total	died (28d)	(%)
hospital-	0-39	517	23	4.4%
onset	40-49	496	65	13.1%
indeterminate	50-59	975	180	18.5%
healthcare-	60-64	611	145	23.7%
associated	65-69	683	207	30.3%
	70-74	894	308	34.5%
	75-79	1070	454	42.4%
	80-84	1263	526	41.6%
	85-89	1222	598	48.9%
	90+	948	497	52.4%
	Total	8,679	3,003	34.6%

HO.pHA	age (years)	total	died (28d)	(%)
hospital-	0-39	144	12	8.3%
onset	40-49	179	28	15.6%
probable	50-59	398	96	24.1%
healthcare-	60-64	294	103	35.0%
associated	65-69	437	148	33.9%
	70-74	708	320	45.2%
	75-79	829	375	45.2%
	80-84	1148	551	48.0%
	85-89	1256	643	51.2%
	90+	1042	564	54.1%
	Total	6,435	2,840	44.1%

HO.HA	age (years)	total	died (28d)	(%)
hospital-	0-39	268	12	4.5%
onset	40-49	238	31	13.0%
definite	50-59	542	118	21.8%
healthcare-	60-64	396	114	28.8%
associated	65-69	529	180	34.0%
	70-74	798	306	38.3%
	75-79	999	417	41.7%
	80-84	1357	594	43.8%
	85-89	1346	637	47.3%
	90+	967	477	49.3%
	Total	7,440	2,886	38.8%

HO.pHA	age (years)	total	died (28d)	(%)
and	0-39	412	24	5.8%
HO.HA	40-49	417	59	14.1%
	50-59	940	214	22.8%
	60-64	690	217	31.4%
	65-69	966	328	34.0%
	70-74	1506	626	41.6%
	75-79	1828	792	43.3%
	80-84	2505	1145	45.7%
	85-89	2602	1280	49.2%
	90+	2009	1041	51.8%
	Total	13,875	5726	41.3%

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE JANSSEN COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Janssen COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 18 years of age and older.

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults, and cases of COVID-19 that result in hospitalization or death following administration of the Janssen COVID-19 Vaccine. See "MANDATORY REQUIREMENTS FOR THE JANSSEN COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

The Janssen COVID-19 Vaccine is a suspension for intramuscular injection.

Primary Vaccination

The primary vaccination regimen for the Janssen COVID-19 Vaccine is a **single-dose** (0.5 mL) administered to individuals 18 years of age and older.

Booster Dose

A single Janssen COVID-19 Vaccine booster dose (0.5 mL) may be administered at least 2 months after primary vaccination with the Janssen COVID-19 Vaccine, to individuals 18 years of age and older.

A single booster dose of the Janssen COVID-19 Vaccine (0.5 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.janssencovid19vaccine.com.

For information on clinical trials that are testing the use of the Janssen COVID-19 Vaccine for active immunization against COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild

symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

The storage and handling information in this Fact Sheet supersedes the storage and handling information on the carton and vial labels.

Storage and Handling

Storage Prior to First Puncture of the Vaccine Vial

Store unpunctured multi-dose vials of the Janssen COVID-19 Vaccine at 2°C to 8°C (36°F to 46°F) and protect from light. Do not store frozen.

Unpunctured vials of Janssen COVID-19 Vaccine may be stored between 9°C to 25°C (47°F to 77°F) for up to 12 hours.

The Janssen COVID-19 Vaccine is initially stored frozen by the manufacturer, then shipped at 2°C to 8°C (36°F to 46°F). If vaccine is still frozen upon receipt, thaw at 2°C to 8°C (36°F to 46°F). If needed immediately, thaw at room temperature (maximally 25°C/77°F). At room temperature (maximally 25°C/77°F), a carton of 10 vials will take approximately 4 hours to thaw, and an individual vial will take approximately 1 hour to thaw. Do not refreeze once thawed.

Storage After First Puncture of the Vaccine Vial

After the first dose has been withdrawn, hold the vial between 2° to 8°C (36° to 46°F) for up to 6 hours or at room temperature (maximally 25°C/77°F) for up to 2 hours. Discard the vial if vaccine is not used within these times.

Dosing and Schedule

Primary Vaccination

The primary vaccination regimen for the Janssen COVID-19 Vaccine is a single-dose (0.5 mL) administered to individuals 18 years of age and older.

Booster Dose

A single Janssen COVID-19 Vaccine booster dose (0.5 mL) may be administered at least 2 months after primary vaccination with the Janssen COVID-19 Vaccine, to individuals 18 years of age and older.

A single booster dose of the Janssen COVID-19 Vaccine (0.5 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

Dose Preparation

- The Janssen COVID-19 Vaccine is a colorless to slightly yellow, clear to very opalescent suspension. Visually inspect the Janssen COVID-19 Vaccine vials for particulate matter and discoloration prior to administration. If either of these conditions exists, do not administer the vaccine.
- Before withdrawing each dose of vaccine, carefully mix the contents of the multi-dose vial by swirling gently in an upright position for 10 seconds. **Do not shake**.
- Each dose is 0.5 mL. Each vial contains five doses. Do not pool excess vaccine from multiple vials.
- The Janssen COVID-19 Vaccine does not contain a preservative. Record the date and time of first use on the Janssen COVID-19 Vaccine vial label. After the first dose has been withdrawn, hold the vial between 2° to 8°C (36° to 46°F) for up to 6 hours or at room temperature (maximally 25°C/77°F) for up to 2 hours. Discard if vaccine is not used within these times.

Administration

Visually inspect each dose in the dosing syringe prior to administration. The Janssen COVID-19 Vaccine is a colorless to slightly yellow, clear to very opalescent suspension. During the visual inspection,

- verify the final dosing volume of 0.5 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Janssen COVID-19 Vaccine intramuscularly.

CONTRAINDICATION

Do not administer the Janssen COVID-19 Vaccine to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Janssen COVID-19 Vaccine *(see Full EUA Prescribing Information)*.

WARNINGS

Management of Acute Allergic Reactions

Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Janssen COVID-19 Vaccine.

Monitor Janssen COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Thrombosis with thrombocytopenia

Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of thrombosis involving the cerebral venous sinuses and other sites (including but not limited to the large blood vessels of the abdomen and the veins of the lower extremities) combined with thrombocytopenia and with onset of symptoms approximately one to two weeks after vaccination. The reporting rate of thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine has been highest in females ages 18 through 49 years; some cases have been fatal. The clinical course of these events shares features with autoimmune heparin-induced thrombocytopenia. In individuals with suspected thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine, the use of heparin may be harmful and alternative treatments may be needed. Consultation with hematology specialists is strongly recommended. The American Society of Hematology has published considerations relevant to the diagnosis and treatment of thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine (*https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia*). *(see Full EUA Prescribing Information)*.

Guillain-Barré Syndrome

Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of Guillain-Barré syndrome during the 42 days following vaccination.

Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Janssen COVID-19 Vaccine.

Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

Limitations of Vaccine Effectiveness

The Janssen COVID-19 Vaccine may not protect all vaccinated individuals.

ADVERSE REACTIONS

Adverse Reactions in Clinical Trials

Adverse reactions reported in a clinical trial following administration of the Janssen COVID-19 Vaccine include injection site pain, headache, fatigue, myalgia, nausea, fever, injection site erythema and injection site swelling. In clinical studies, severe allergic reactions, including anaphylaxis, have been reported following administration of the Janssen COVID-19 Vaccine *(see Full EUA Prescribing Information)*.

Adverse Reactions Identified during Post Authorization Use

Anaphylaxis and other severe allergic reactions, thrombosis with thrombocytopenia, Guillain-Barré syndrome, and capillary leak syndrome have been reported following

administration of the Janssen COVID-19 Vaccine during mass vaccination outside of clinical trials.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Janssen COVID-19 Vaccine.

USE WITH OTHER VACCINES

There is no information on the co-administration of the Janssen COVID-19 Vaccine with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.janssencovid19vaccine.com to obtain the Fact Sheet) prior to the individual receiving the Janssen COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Janssen COVID-19 Vaccine, which is not an FDA approved vaccine.
- The recipient or their caregiver has the option to accept or refuse the Janssen COVID-19 Vaccine.
- The significant known and potential risks and benefits of the Janssen COVID-19 Vaccine, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are testing the use of the Janssen COVID-19 Vaccine to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the name of the vaccine ("Janssen COVID-19 Vaccine") and date of administration to document vaccination.

Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR JANSSEN COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of the Janssen COVID-19 Vaccine, the following items are required. Use of

unapproved Janssen COVID-19 Vaccine for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements must be met):

1. The Janssen COVID-19 Vaccine is authorized for use in individuals 18 years of age and older.

2. The vaccination provider must communicate to the individual receiving the Janssen COVID-19 Vaccine or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" prior to the individual receiving the Janssen COVID-19 Vaccine.

3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):

   - vaccine administration errors whether or not associated with an adverse event,
   - serious adverse events* (irrespective of attribution to vaccination),
   - cases of Multisystem Inflammatory Syndrome (MIS) in adults, and
   - cases of COVID-19 that result in hospitalization or death.

   Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS, call 1-800-822-7967. The reports should include the words "Janssen COVID-19 Vaccine EUA" in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of MIS in adults, and cases of COVID-19 that result in hospitalization or death following administration of the Janssen COVID-19 Vaccine to recipients.

   * Serious adverse events are defined as:
   - Death;
   - A life-threatening adverse event;
   - Inpatient hospitalization or prolongation of existing hospitalization;
   - A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
   - A congenital anomaly/birth defect;
   - An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND JANSSEN BIOTECH, INC.

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

Revised: Oct/20/2021

To the extent feasible, report adverse events to Janssen Biotech, Inc. using the contact information below or by providing a copy of the VAERS form to Janssen Biotech, Inc:

e-mail	Fax number	Telephone numbers
JNJvaccineAE@its.jnj.com	215-293-9955	US Toll Free: 1-800-565-4008 US Toll: (908) 455-9922

ADDITIONAL INFORMATION

For general questions or to access the most recent Janssen COVID-19 Vaccine Fact Sheets, scan the QR code using your device, visit www.janssencovid19vaccine.com or call the telephone numbers provided below.

QR Code	Fact Sheets Website	Telephone numbers
	www.janssencovid19vaccine.com.	US Toll Free: 1-800-565-4008 US Toll: 1-908-455-9922

AVAILABLE ALTERNATIVES

Comirnaty (COVID-19 Vaccine, mRNA) is an FDA-approved vaccine to prevent COVID-19 caused by SARS-CoV-2. There may be clinical trials or availability under EUA of other COVID-19 vaccines.

FEDERAL COVID-19 VACCINATION PROGRAM

This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, HRSA COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see *https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html*.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19

pandemic. In response, FDA has issued an EUA for the unapproved product, Janssen COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 18 years of age and older.

FDA issued this EUA, based on Janssen Biotech, Inc.'s request and submitted data.

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Janssen COVID-19 Vaccine may be effective for the prevention of COVID-19 in individuals as specified in the Full EUA Prescribing Information.

This EUA for the Janssen COVID-19 Vaccine will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

THE COUNTERMEASURES INJURY COMPENSATION PROGRAM

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP, visit www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Manufactured by:
Janssen Biotech, Inc.
a Janssen Pharmaceutical Company of Johnson & Johnson
Horsham, PA 19044, USA

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

END SHORT VERSION FACT SHEET
Long Version (Full EUA Prescribing Information) Begins On Next Page

Revised: Oct/20/2021

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION JANSSEN COVID-19 VACCINE

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

Revised: Oct/20/2021

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

Janssen COVID-19 vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

- The Janssen COVID-19 Vaccine is a colorless to slightly yellow, clear to very opalescent suspension. Visually inspect the Janssen COVID-19 Vaccine vials for particulate matter and discoloration prior to administration. If either of these conditions exists, do not administer the vaccine.
- Before withdrawing each dose of vaccine, carefully mix the contents of the multi-dose vial by swirling gently in an upright position for 10 seconds. **Do not shake**.
- Each dose is 0.5 mL. Each vial contains five doses. Do not pool excess vaccine from multiple vials.
- The Janssen COVID-19 Vaccine does not contain a preservative. Record the date and time of first use on the Janssen COVID-19 Vaccine vial label. After the first dose has been withdrawn, hold the vial between 2° to 8°C (36° to 46°F) for up to 6 hours or at room temperature (maximally 25°C/77°F) for up to 2 hours. Discard if vaccine is not used within these times.

2.2 Administration

Visually inspect each dose in the dosing syringe prior to administration. The Janssen COVID-19 Vaccine is a colorless to slightly yellow, clear to very opalescent suspension. During the visual inspection,

- verify the final dosing volume of 0.5 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Janssen COVID-19 Vaccine intramuscularly.

2.3 Dosing and Schedule

Primary Vaccination

The primary vaccination regimen for the Janssen COVID-19 Vaccine is a single-dose (0.5 mL) administered to individuals 18 years of age and older.

Booster Dose

A single Janssen COVID-19 Vaccine booster dose (0.5 mL) may be administered at least 2 months after primary vaccination with the Janssen COVID-19 Vaccine, to individuals 18 years of age and older.

A single booster dose of the Janssen COVID-19 Vaccine (0.5 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

3 DOSAGE FORMS AND STRENGTHS

Janssen COVID-19 Vaccine is a suspension for intramuscular injection. A single-dose is 0.5 mL.

4 CONTRAINDICATIONS

Do not administer the Janssen COVID-19 Vaccine to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of the Janssen COVID-19 Vaccine *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Janssen COVID-19 Vaccine.

Monitor Janssen COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (*https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html*).

5.2 Thrombosis with thrombocytopenia

Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of thrombosis involving the cerebral venous sinuses and other sites (including but not limited to the large blood vessels of the abdomen and the veins of the lower extremities) combined with thrombocytopenia and with onset of symptoms approximately one to two weeks after vaccination *[see Overall Safety Summary (6.2)]*. The reporting rate of thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine has been highest in females ages 18 through 49 years; some cases have been fatal. The clinical course of these events shares features with autoimmune heparin-induced thrombocytopenia.

Specific risk factors for thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine and the level of potential excess risk due to vaccination are under investigation. Based on currently available evidence, a causal relationship between thrombosis with thrombocytopenia and the Janssen COVID-19 Vaccine is plausible.

Healthcare professionals should be alert to the signs and symptoms of thrombosis with thrombocytopenia in individuals who receive the Janssen COVID-19 Vaccine. In individuals with suspected thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine, the use of heparin may be harmful and alternative treatments may be needed. Consultation with hematology specialists is strongly recommended. The American Society of Hematology has published considerations relevant to the diagnosis and treatment of thrombosis with thrombocytopenia following administration of the Janssen COVID-19 Vaccine (*https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia*).

Recipients of Janssen COVID-19 Vaccine should be instructed to seek immediate medical attention if they develop shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurological symptoms (including severe or persistent headaches or blurred vision), or petechiae beyond the site of vaccination.

5.3 Guillain-Barré Syndrome

Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of Guillain-Barré syndrome during the 42 days following vaccination.

5.4 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

5.5 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Janssen COVID-19 Vaccine.

5.6 Limitations of Vaccine Effectiveness

The Janssen COVID-19 Vaccine may not protect all vaccinated individuals.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults, and hospitalized or fatal cases of COVID-19 following vaccination with the Janssen COVID-19 Vaccine. To the extent feasible, provide a copy of the VAERS form to Janssen Biotech, Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS or Janssen Biotech, Inc.

Adverse Reactions in Clinical Trials

In study COV3001, the most common local solicited adverse reaction (≥10%) reported was injection site pain (48.6%). The most common systemic adverse reactions (≥10%) were headache (38.9%), fatigue (38.2%), myalgia (33.2%), and nausea (14.2%) (see Tables 1 to 4).

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Janssen COVID-19 vaccine.

Adverse Reactions Identified during Post Authorization Use

Anaphylaxis and other severe allergic reactions, thrombosis with thrombocytopenia, Guillain-Barré syndrome, and capillary leak syndrome have been reported following administration of the Janssen COVID-19 Vaccine during mass vaccination outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Safety Primary vaccination

The safety of the Janssen COVID-19 Vaccine has been assessed in an ongoing Phase 3 Study, COV3001 (NCT04505722) (Study 1). A total of 43,783 individuals were enrolled in this study, of whom 21,895 adults aged 18 years and older received the Janssen COVID-19 Vaccine [Full Analysis Set (FAS)]. This study is being conducted in the United States (n=19,302), Brazil (n=7,278), South Africa (n=6,576), Colombia (n=4,248), Argentina (n=2,996), Peru (n=1,771), Chile (n=1,133), Mexico (n=479). In this study, 45.0% were female, 54.9% were male, 58.7% were White, 19.4% were Black or African American, 45.3% were Hispanic or Latino, 3.3% were Asian, 9.5% were American Indian/Alaska Native and 0.2% were Native Hawaiian or other Pacific Islander, 5.6% were from multiple racial groups and 1.4% were unknown races (see Table 5). The median age of individuals was 52.0 years (range: 18-100). There were 4,217 (9.6%) individuals who were SARS-CoV-2 seropositive at baseline and who were included in the study. In the United States, 838 of 19,302 (4.3%) individuals were SARS-CoV-2 seropositive. Demographic characteristics were similar among individuals who received the Janssen COVID-19 Vaccine and those who received saline placebo.

The safety subset includes 6,736 individuals (3,356 from the Janssen COVID-19 Vaccine group, 3,380 from the placebo group). The demographic profile in the safety subset was similar in terms of age and gender compared to the FAS. A larger percentage of individuals in the safety subset were White (83.4%) compared to the FAS (58.7%). Geographically, the safety subset was limited to individuals from the United States (51.4%), Brazil (38.5%) and South Africa (10.2%). Fewer individuals in the safety subset compared to the FAS were SARS-CoV-2 seropositive at baseline, 4.5% vs. 9.6%, and had at least one comorbidity 34.1% vs 40.8%.

Safety monitoring in the clinical study consisted of monitoring for: (1) solicited local and systemic reactions occurring in the 7 days following vaccination in a subset of individuals (safety subset),

(2) unsolicited adverse events (AEs) occurring in the 28 days following vaccination in the safety subset, (3) medically-attended AEs (MAAEs) occurring in the 6 months following vaccination in the entire study population (FAS), (4) serious AEs (SAEs) and AEs leading to study discontinuation for the duration of the study in the entire study population.

Solicited adverse reactions

Shown below are the frequencies of solicited local adverse reactions (Tables 1 and 2) and systemic adverse reactions (Tables 3 and 4) reported in adults by age group in the 7 days following vaccination in Study 1.

Table 1: Study 1: Solicited Local Adverse Reactions Reported in the 7 Days Following Primary Vaccination - Individuals 18 to 59 Years of Age

Adverse Reactions	Janssen COVID-19 Vaccine N=2,036 n(%)	Placebo N=2,049 n(%)
Injection Site Pain		
Any	1,193 (58.6)	357 (17.4)
Grade 3[a]	8 (0.4)	0
Injection Site Erythema		
Any (≥25 mm)	184 (9.0)	89 (4.3)
Grade 3[b]	6 (0.3)	2 (0.1)
Injection Site Swelling		
Any (≥25 mm)	142 (7.0)	32 (1.6)
Grade 3[b]	5 (0.2)	2 (0.1)

[a] Grade 3 injection site pain: Defined as incapacitating symptoms; inability to do work, school, or usual activities; use of narcotic pain reliever.

[b] Grade 3 injection site swelling and erythema: Defined as >100 mm.

Table 2: Study 1: Solicited Local Adverse Reactions Reported in the 7 Days Following Primary Vaccination - Individuals 60 Years of Age and Older

Adverse Reactions	Janssen COVID-19 Vaccine N=1,320 n(%)	Placebo N=1,331 n(%)
Injection Site Pain		
Any	439 (33.3)	207 (15.6)
Grade 3[a]	3 (0.2)	2 (0.2)
Injection Site Erythema		
Any (≥25 mm)	61 (4.6)	42 (3.2)
Grade 3[b]	1 (0.1)	0
Injection Site Swelling		
Any (≥25 mm)	36 (2.7)	21 (1.6)
Grade 3[b]	2 (0.2)	0

[a] Grade 3 injection site pain: Defined as incapacitating symptoms; inability to do work, school, or usual activities; use of narcotic pain reliever.

[b] Grade 3 injection site swelling and erythema: Defined as >100 mm.

Table 3: Study 1: Solicited Systemic Adverse Reactions Reported in the 7 Days Following Primary Vaccination - Individuals 18 to 59 Years of Age

Adverse Reactions	Janssen COVID-19 Vaccine N=2,036 n(%)	Placebo N=2,049 n(%)
Headache		
Any	905 (44.4)	508 (24.8)
Grade 3[a]	18 (0.9)	5 (0.2)
Fatigue		
Any	891 (43.8)	451 (22.0)
Grade 3[b]	25 (1.2)	4 (0.2)
Myalgia		
Any	796 (39.1)	248 (12.1)
Grade 3[b]	29 (1.4)	1 (<0.1)
Nausea		
Any	315 (15.5)	183 (8.9)
Grade 3[b]	3 (0.1)	3 (0.1)
Fever[c]		
Any	261 (12.8)	14 (0.7)
Grade 3	7 (0.3)	0
Use of antipyretic or pain medication	538 (26.4)	123 (6.0)

[a] Grade 3 headache: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

[b] Grade 3 fatigue, myalgia, nausea: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

[c] Fever of any grade: Defined as body temperature ≥38°C/100.4°F. Grade 3 fever: Defined as 39.0°C - 40.0°C (102.1°F - 104.0°F).

Table 4: Study 1: Solicited Systemic Adverse Reactions Reported in the 7 Days Following Primary Vaccination - Individuals 60 Years of Age and Older

Adverse Reactions	Janssen COVID-19 Vaccine N=1,320 n(%)	Placebo N=1,331 n(%)
Headache		
Any	401 (30.4)	294 (22.1)
Grade 3[a]	5 (0.4)	4 (0.3)
Fatigue		
Any	392 (29.7)	277 (20.8)
Grade 3[b]	10 (0.8)	5 (0.4)
Myalgia		
Any	317 (24.0)	182 (13.7)
Grade 3[b]	3 (0.2)	5 (0.4)
Nausea		
Any	162 (12.3)	144 (10.8)
Grade 3[b]	3 (0.2)	3 (0.2)
Fever[c]		
Any	41 (3.1)	6 (0.5)
Grade 3	1 (0.1)	0
Use of antipyretic or pain medication	130 (9.8)	68 (5.1)

[a] Grade 3 headache: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever

[b] Grade 3 fatigue, myalgia, nausea: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

[c] Fever of any grade: Defined as body temperature ≥38°C/100.4°F. Grade 3 fever: Defined as 39.0°C - 40.0°C (102.1°F - 104.0°F).

Solicited local and systemic adverse reactions reported following administration of the Janssen COVID-19 Vaccine had a median duration of 1 to 2 days.

Unsolicited adverse events

Individuals within the safety subset in Study 1 (N=6,736) were monitored for unsolicited adverse events (AEs) for 28 days following vaccination with 99.9% (N= 6,730) of individuals completing the full 28 days of follow-up. The proportion of individuals who reported one or more unsolicited AEs was similar among those in the Janssen COVID-19 Vaccine group (13.1%) and those in the placebo group (12.0%).

Serious Adverse Events (SAEs) and other events of interest

In Study 1, up to a cut-off date of January 22, 2021, 54.6% of individuals had follow-up duration of 8 weeks. The median follow-up duration for all individuals was 58 days. SAEs, excluding those related to confirmed COVID-19, were reported by 0.4% (n=83) of individuals who received the Janssen COVID-19 Vaccine (N= 21,895) and 0.4% (n=96) of individuals who received placebo (N= 21,888).

Additional adverse events of interest, including but not limited to allergic, neurologic, inflammatory, vascular, and autoimmune disorders, were analyzed among all adverse events collected through protocol-specified safety monitoring procedures as well as unsolicited reporting.

Urticaria (all non-serious) was reported in five vaccinated individuals and 1 individual who received placebo in the 7 days following vaccination. In addition, an SAE of hypersensitivity, not classified as anaphylaxis, was reported in 1 vaccinated individual with urticaria beginning two days following vaccination and angioedema of the lips with no respiratory distress beginning four days following vaccination. The event was likely related to the vaccine.

An SAE of severe pain in the injected arm, not responsive to analgesics, with immediate onset at time of vaccination, and that was ongoing 74 days following vaccination was reported in an individual who received the Janssen COVID-19 Vaccine. An SAE of severe generalized weakness, fever, and headache, with onset on the day following vaccination and resolution three days following vaccination was reported in an individual who received the Janssen COVID-19 Vaccine. Both SAEs are likely related to the vaccine.

Numerical imbalances, with more events in vaccine than placebo recipients, were observed for the following serious and other adverse events of interest in individuals receiving the vaccine or placebo, respectively:

- Thromboembolic events:
  - Deep vein thrombosis: 6 events (2 serious; 5 within 28 days of vaccination) vs. 2 events (1 serious; 2 within 28 days of vaccination).
  - Pulmonary embolism: 4 events (3 serious; 2 within 28 days of vaccination) vs. 1 event (serious and within 28 days of vaccination).
  - Transverse sinus thrombosis with thrombocytopenia: 1 event (serious, with onset of symptoms 8 days post- vaccination) vs. 0.

- Seizures: 4 events (1 serious; 4 within 28 days of vaccination) vs. 1 event (0 serious and 0 within 28 days following vaccination).

- Tinnitus: 6 events (0 serious; 6 within 28 days of vaccination, including 3 within 2 days of vaccination) vs. 0.

For these events, a causal relationship with the Janssen COVID-19 vaccine could not be determined based on Study 1. The assessment of causality was confounded by the presence of underlying medical conditions that may have predisposed individuals to these events. However, taking into consideration post-authorization experience, a causal relationship with Janssen COVID-19 Vaccine is plausible for thrombosis with thrombocytopenia *[see Warnings and Precautions (5.2) and Overall Safety Summary (6.2)]*.

There were no additional notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and cardiovascular events) that would suggest a causal relationship to the Janssen COVID-19 Vaccine.

Booster Dose Following Primary Vaccination with Janssen COVID-19 Vaccine

Overall, in 5 clinical studies conducted in Belgium, Brazil, Colombia, France, Germany, Japan, Netherlands, Philippines, South Africa, Spain, United Kingdom and United States, approximately 9,000 participants have received 2 doses of the Janssen COVID-19 Vaccine, administered at least 2 months apart and approximately 2,700 participants had at least 2 months of safety follow-up after the booster dose.

A randomized, double-blind, placebo-controlled Phase 2 study, COV2001 (NCT04535453) (Study 2), evaluated the frequency and severity of local and systemic adverse reactions within 7 days of administration of a booster dose of the Janssen COVID-19 Vaccine administered approximately 2 months after the primary vaccination in healthy adults 18 through 55 years of age and adults 65 years and older in good or stable health. A total of 141 individuals received at least one dose of the vaccine and 137 received both the primary vaccination and the booster dose at an interval of 2 months. The median age of individuals was 48 years, and 48 individuals (34%) were 65 years of age and older. Data on solicited adverse reactions after the primary vaccination and after a booster dose are shown in Tables 5-8.

Solicited adverse reactions

Table 5: Study 2 - Solicited Local Adverse Reactions Reported in the 7 Days Following the Primary Vaccination or the Booster Dose - Individuals 18 through 55 Years of Age

Adverse Reactions	Primary Vaccination N=93 n(%)	Booster Dose N=89 n(%)
Injection Site Pain		
Any	58 (62.4%)	53 (59.6%)
Grade 3[a]	0	1 (1.1%)
Injection Site Erythema		
Any (≥25 mm)	1 (1.1%)	1 (1.1%)
Grade 3[b]	0	0
Injection Site Swelling		
Any (≥25 mm)	1 (1.1%)	0
Grade 3[b]	0	0

[a] Grade 3 injection site pain: Defined as incapacitating symptoms; inability to do work, school, or usual activities; use of narcotic pain reliever.

[b] Grade 3 injection site swelling and erythema: Defined as >100 mm.

Table 6: Study 2 - Solicited Local Adverse Reactions Reported in the 7 Days Following the Primary Vaccination or the Booster Dose - Individuals 65 Years of Age and Older

Adverse Reactions	Primary Vaccination N=48 n(%)	Booster Dose N=48 n(%)
Injection Site Pain		
Any	17 (35.4%)	10 (20.8%)
Grade 3[a]	0	0
Injection Site Erythema		
Any (≥25 mm)	0	0
Grade 3[b]	0	0
Injection Site Swelling		
Any (≥25 mm)	0	0
Grade 3[b]	0	0

[a] Grade 3 injection site pain: Defined as incapacitating symptoms; inability to do work, school, or usual activities; use of narcotic pain reliever.

[b] Grade 3 injection site swelling and erythema: Defined as >100 mm.

Table 7: Study 2 - Solicited Systemic Adverse Reactions Reported in the 7 Days Following the Primary Vaccination or the Booster Dose - Individuals 18 through 55 Years of Age

Adverse Reactions	Primary Vaccination N=93 n(%)	Booster Dose N=89 n(%)
Headache		
Any	49 (52.7%)	37 (41.6%)
Grade 3[a]	2 (2.2%)	1 (1.1%)
Fatigue		
Any	55 (59.1%)	46 (51.7%)
Grade 3[b]	1 (1.1%)	0
Myalgia		
Any	44 (47.3%)	32 (36.0%)
Grade 3[b]	3 (3.2%)	2 (2.2%)
Nausea		
Any	13 (14.0%)	9 (10.1%)
Grade 3[b]	1 (1.1%)	0
Fever[c]		
Any	13 (14.0%)	5 (5.6%)
Grade 3	1 (1.1%)	0

a Grade 3 headache: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

b Grade 3 fatigue, myalgia, nausea: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

c Fever of any grade: Defined as body temperature ≥38°C/100.4°F. Grade 3 fever: Defined as 39.0°C - 40.0°C (102.1°F - 104.0°F).

Table 8: Study 2 - Solicited Systemic Adverse Reactions Reported in the 7 Days Following the Primary Vaccination or the Booster Dose - Individuals 65 Years of Age and Older

Adverse Reactions	Primary Vaccination N=48 n(%)	Booster Dose N=48 n(%)
Headache		
Any	**9 (18.8%)**	**13 (27.1%)**
Grade 3[a]	**0**	**0**
Fatigue		
Any	9 (18.8%)	16 (33.3%)
Grade 3[b]	0	0
Myalgia		
Any	4 (8.3%)	5 (10.4%)
Grade 3[b]	0	0
Nausea		
Any	0	1 (2.1%)
Grade 3[b]	0	0
Fever[c]		
Any	1 (2.1%)	0
Grade 3	0	0

a Grade 3 headache: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever

b Grade 3 fatigue, myalgia, nausea: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

c Fever of any grade: Defined as body temperature ≥38°C/100.4°F. Grade 3 fever: Defined as 39.0°C - 40.0°C (102.1°F - 104.0°F).

Unsolicited adverse events

An overall assessment of Janssen's safety analyses from studies evaluating 2 doses of Janssen COVID-19 Vaccine did not reveal new safety concerns following a booster dose, as compared with adverse reactions reported following the single-dose primary vaccination.

Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

The safety of a Janssen COVID-19 Vaccine booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 Vaccine (heterologous booster dose) is inferred from the safety of a Janssen COVID-19 Vaccine booster dose administered following completion of Janssen COVID-19 Vaccine primary vaccination (homologous booster dose) and from data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the Janssen COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Janssen COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following a Janssen COVID-19 Vaccine primary vaccination or homologous booster dose.

6.2 Post Authorization Experience

The following adverse reactions have been identified during post-authorization use of the Janssen COVID-19 Vaccine. Because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Blood and Lymphatic System Disorders: Thrombosis with thrombocytopenia, Lymphadenopathy, Immune thrombocytopenic purpura.

Cardiac disorders: Myocarditis, Pericarditis.

Ear and labyrinth disorders: Tinnitus.

Gastrointestinal disorders: Diarrhea, Vomiting.

Immune System Disorders: Allergic reactions, including anaphylaxis.

Nervous System Disorders: Guillain-Barré syndrome, Syncope, Paresthesia, Hypoesthesia.

Vascular Disorders: Capillary leak syndrome, Thrombosis with thrombocytopenia, Venous thromboembolism (with or without thrombocytopenia).

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following Janssen COVID-19 Vaccine administration to the Vaccine Adverse Event Reporting System (VAERS):

- Vaccine administration errors whether or not associated with an adverse event,
- Serious adverse events* (irrespective of attribution to vaccination),
- Cases of Multisystem Inflammatory Syndrome (MIS) in adults,
- Cases of COVID-19 that result in hospitalization or death.

  * Serious Adverse Events are defined as:
  - Death;
  - A life-threatening adverse event;
  - Inpatient hospitalization or prolongation of existing hospitalization;
  - A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
  - A congenital anomaly/birth defect;
  - An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using one of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics, (e.g., patient name, date of birth),
- Pertinent medical history,
- Pertinent details regarding admission and course of illness,
- Concomitant medications,

- Timing of adverse event(s) in relationship to administration of Janssen COVID-19 vaccine,
- Pertinent laboratory and virology information,
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on Janssen COVID-19 Vaccine and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.
2. In Box 18, description of the event:
   a. Write "Janssen COVID-19 Vaccine EUA" as the first line.
   b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
   a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
   b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.
   c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Janssen Biotech, Inc. using the contact information below or by providing a copy of the VAERS form to Janssen Biotech, Inc:

e-mail	Fax number	Telephone numbers
JNJvaccineAE@its.jnj.com	215-293-9955	US Toll Free: 1-800-565-4008 US Toll: (908) 455-9922

10 DRUG INTERACTIONS

There are no data to assess the concomitant administration of the Janssen COVID-19 Vaccine with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Janssen COVID-19 Vaccine during pregnancy. Women who are vaccinated with Janssen COVID-19 Vaccine during pregnancy are encouraged to enroll in the registry by visiting https://c-viper.pregistry.com.

Risk Summary

All Pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Available data on Janssen COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a reproductive developmental toxicity study female rabbits were administered 1 mL of the Janssen COVID-19 Vaccine (a single human dose is 0.5 mL) by intramuscular injection 7 days prior to mating and on Gestation Days 6 and 20 (i.e., one vaccination during early and late gestation, respectively). No vaccine related adverse effects on female fertility, embryo-fetal or postnatal development up to Postnatal Day 28 were observed.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Janssen COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Emergency Use Authorization of the Janssen COVID-19 Vaccine does not include use in individuals younger than 18 years of age.

11.4 Geriatric Use

Clinical studies of Janssen COVID-19 Vaccine included individuals 65 years of age and older and their data contributes to the overall assessment of safety and efficacy *[see Overall Safety Summary (6.1) and Clinical Trial Results and Supporting Data for EUA (18)]*. Of the 21,895 individuals who received a single-dose of the Janssen COVID-19 Vaccine in COV3001, 19.5% (n=4,259) were 65 years of age and older and 3.7% (n=809) were 75 years of age and older. No overall differences in safety or efficacy were observed between individuals 65 years of age and older and younger individuals.

13 DESCRIPTION

The Janssen COVID-19 Vaccine is a colorless to slightly yellow, clear to very opalescent sterile suspension for intramuscular injection. It contains no visible particulates. The vaccine consists of a replication-incompetent recombinant adenovirus type 26 (Ad26) vector expressing the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike (S) protein in a stabilized conformation.

The Ad26 vector expressing the SARS-CoV-2 S protein is grown in PER.C6 TetR cells, in media containing amino acids and no animal-derived proteins. After propagation, the vaccine is processed through several purification steps, formulated with inactive ingredients and filled into vials.

Each 0.5 mL dose of Janssen COVID-19 Vaccine is formulated to contain 5×10^{10} virus particles (VP) and the following inactive ingredients: citric acid monohydrate (0.14 mg), trisodium citrate dihydrate (2.02 mg), ethanol (2.04 mg), 2-hydroxypropyl-β-cyclodextrin (HBCD) (25.50 mg), polysorbate-80 (0.16 mg), sodium chloride (2.19 mg). Each dose may also contain residual amounts of host cell proteins (≤0.15 mcg) and/or host cell DNA (≤3 ng).

Janssen COVID-19 Vaccine does not contain a preservative.

The vial stoppers are not made with natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The Janssen COVID-19 Vaccine is composed of a recombinant, replication-incompetent human adenovirus type 26 vector that, after entering human cells, expresses the SARS-CoV-2 spike (S) antigen without virus propagation. An immune response elicited to the S antigen protects against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Efficacy of Primary Vaccination

A primary analysis (cut-off date January 22, 2021) of a multicenter, randomized, double-blind, placebo-controlled Phase 3 Study (Study 1) was conducted in the United States, South Africa, Brazil, Chile, Argentina, Colombia, Peru and Mexico to assess the efficacy, safety, and immunogenicity of a single-dose of the Janssen COVID-19 Vaccine for the prevention of COVID-19 in adults aged 18 years and older. Randomization was stratified by age (18-59 years, 60 years and older) and presence or absence of comorbidities associated with an increased risk of progression to severe COVID-19. The study allowed for the inclusion of individuals with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy during the 3 months preceding vaccination, as well as individuals with stable human immunodeficiency virus (HIV) infection.

A total of 44,325 individuals were randomized equally to receive Janssen COVID-19 Vaccine or saline placebo. Individuals are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The primary efficacy analysis population of 39,321 individuals (19,630 in the Janssen COVID-19 Vaccine group and 19,691 in the placebo group) included 38,059 SARS-CoV-2 seronegative individuals at baseline and 1,262 individuals with an unknown serostatus. Demographic and baseline characteristics were similar among individuals who received the Janssen COVID-19 Vaccine and those who received placebo (see Table 9).

Table 9: Summary of Demographics and Baseline Characteristics - Primary Efficacy Analysis Population

	Janssen COVID-19 Vaccine (N=19,630) n (%)	Placebo (N=19,691) n (%)
Sex		
Male	10,924 (55.6)	10,910 (55.4)
Female	8,702 (44.3)	8,777 (44.6)
Age (years)		
Mean (SD)	51.1 (15.0)	51.2 (15.0)
Median	52.0	53.0
Min, max	(18; 100)	(18; 94)
Age group		
≥18 to 59 years of age	12,830 (65.4)	12,881 (65.4)
≥60 years of age	6,800 (34.6)	6,810 (34.6)
≥65 years of age	3,984 (20.3)	4,018 (20.4)
≥75 years of age	755 (3.8)	693 (3.5)
Race[a]		
White	12,200 (62.1)	12,216 (62.0)
Black or African American	3,374 (17.2)	3,390 (17.2)
Asian	720 (3.7)	663 (3.4)
American Indian/Alaska Native[b]	1,643 (8.4)	1,628 (8.3)
Native Hawaiian or other Pacific Islander	54 (0.3)	45 (0.2)
Multiple	1,036 (5.3)	1,087 (5.5)
Unknown	262 (1.3)	272 (1.4)
Not reported	341 (1.7)	390 (2.0)
Ethnicity		
Hispanic or Latino	8,793 (44.8)	8,936 (45.4)
Not Hispanic or Latino	10,344 (52.7)	10,259 (52.1)
Unknown	173 (0.9)	162 (0.8)
Not reported	319 (1.6)	333 (1.7)
Region		
Northern America (United States)	9,185 (46.8)	9,171 (46.6)
Latin America	7,967 (40.6)	8,014 (40.7)
Southern Africa (South Africa)	2,478 (12.6)	2,506 (12.7)
Comorbidities[c]		
Yes	7,830 (39.9)	7,867 (40.0)
No	11,800 (60.1)	11,824 (60.0)

[a] Some individuals could be classified in more than one category.

[b] Including 175 individuals in the United States, which represents 1% of the population recruited in the United States.

[c] Number of individuals who have 1 or more comorbidities at baseline that increase the risk of progression to severe/critical COVID-19: Obesity defined as BMI ≥30 kg/m^2 (27.5%), hypertension (10.3%), type 2 diabetes (7.2%), stable/well-controlled HIV infection (2.5%), serious heart conditions (2.4%), asthma (1.3%), and in ≤1% of individuals: cancer, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, cystic fibrosis, immunocompromised state (weakened immune system) from blood or organ transplant, liver disease, neurologic conditions, pulmonary fibrosis, sickle cell disease, thalassemia and type 1 diabetes, regardless of age.

Efficacy Against COVID-19

The co-primary endpoints evaluated the first occurrence of moderate to severe/critical COVID-19 with onset of symptoms at least 14 days and at least 28 days after vaccination. Moderate to severe/critical COVID-19 was molecularly confirmed by a central laboratory based on a positive SARS-CoV-2 viral RNA result using a polymerase chain reaction (PCR)-based test.

- Moderate COVID-19 was defined based on the following criteria: the individual must have experienced any one of the following new or worsening signs or symptoms: respiratory rate ≥20 breaths/minute, abnormal saturation of oxygen (SpO2) but still >93% on room air at sea level, clinical or radiologic evidence of pneumonia, radiologic evidence of deep vein thrombosis (DVT), shortness of breath or difficulty breathing OR any two of the following new or worsening signs or symptoms: fever (≥38.0°C or ≥100.4°F), heart rate ≥90 beats/minute, shaking chills or rigors, sore throat, cough, malaise, headache, muscle pain (myalgia), gastrointestinal symptoms, new or changing olfactory or taste disorders, red or bruised appearing feet or toes.

- Severe/critical COVID-19 was defined based on the following criteria: the individual must have experienced any one of the following at any time during the course of observation: clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths/minute, heart rate ≥125 beats/minute, oxygen saturation (SpO2) ≤93% on room air at sea level, or partial pressure of oxygen/fraction of inspired oxygen (PaO2/FiO2) <300 mmHg), respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]), evidence of shock (defined as systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg, or requiring vasopressors), significant acute renal, hepatic, or neurologic dysfunction, admission to intensive care unit (ICU), death.

Final determination of severe/critical COVID-19 cases were made by an independent adjudication committee.

Primary analysis

The median length of follow up for efficacy for individuals in the study was 8 weeks post-vaccination. Vaccine Efficacy (VE) for the co-primary endpoints against moderate to severe/critical COVID-19 in individuals who were seronegative or who had an unknown serostatus at baseline was 66.9% (95% CI: 59.0; 73.4) at least 14 days after vaccination and 66.1% (95% CI: 55.0; 74.8) at least 28 days after vaccination (see Table 10).

Table 10: Analyses of Vaccine Efficacy Against Centrally Confirmed Moderate to Severe/Critical COVID-19 – With Onset at Least 14 Days and at Least 28 Days Post-Vaccination - Primary Efficacy Analysis Population

	Janssen COVID-19 Vaccine N=19,630		Placebo N=19,691		
Subgroup	**COVID-19 Cases (n)**	**Person-Years**	**COVID-19 Cases (n)**	**Person-Years**	**% Vaccine Efficacy (95% CI)**
14 days post-vaccination					
All subjects[a]	116	3116.6	348	3096.1	66.9 (59.0; 73.4)
18 to 59 years of age	95	2106.8	260	2095.0	63.7 (53.9; 71.6)
60 years and older	21	1009.8	88	1001.2	76.3 (61.6; 86.0)
28 days post-vaccination					
All subjects[a]	66	3102.0	193	3070.7	66.1 (55.0; 74.8)[b]
18 to 59 years of age	52	2097.6	152	2077.0	66.1 (53.3; 75.8)
60 years and older	14	1004.4	41	993.6	66.2 (36.7; 83.0)

[a] Co-primary endpoint.
[b] The adjusted CI implements type I error control for multiple testing and is presented upon meeting the prespecified testing conditions.

Vaccine efficacy against severe/critical COVID-19 at least 14 days after vaccination was 76.7% (95% CI: 54.6; 89.1) and 85.4% (95% CI: 54.2; 96.9) at least 28 days after vaccination (see Table 11).

Table 11: Analyses of Vaccine Efficacy: Secondary Endpoints of Centrally Confirmed Severe/Critical COVID-19 – in Adults 18 Years of Age and Older With Onset at Least 14 Days and at Least 28 Days Post-Vaccination – Primary Efficacy Analysis Population

	Janssen COVID-19 Vaccine N=19,630		Placebo N=19,691		
Subgroup	**COVID-19 Cases (n)**	**Person-Years**	**COVID-19 Cases (n)**	**Person-Years**	**% Vaccine Efficacy (95% CI)**
14 days post-vaccination					
Severe/critical	14	3125.1	60	3122.0	76.7 (54.6; 89.1)[a]
28 days post-vaccination					
Severe/critical	5	3106.2	34	3082.6	85.4 (54.2; 96.9)[a]

[a] The adjusted CI implements type I error control for multiple testing and is presented upon meeting the prespecified testing conditions.

Among all COVID-19 cases with onset at least 14 days post vaccination, including cases diagnosed by a positive PCR from a local laboratory and still awaiting confirmation at the central laboratory (as of January 22, 2021), there were 2 COVID-19 related hospitalizations in the vaccine group (with none after 28 days) and 29 in the placebo group (with 16 after 28 days).

As of the primary analysis cut-off date of January 22, 2021, there were no COVID-19-related deaths reported in Janssen COVID-19 Vaccine recipients compared to 5 COVID-19-related deaths reported in placebo recipients, who were SARS-CoV-2 PCR negative at baseline.

Janssen COVID-19 Vaccine Efficacy in Countries With Different Circulating SARS-CoV-2 Variants.

Exploratory subgroup analyses of vaccine efficacy against moderate to severe/critical COVID-19 and severe/critical COVID-19 for Brazil, South Africa, and the United States were conducted (see Table 12). For the subgroup analyses, all COVID-19 cases accrued up to the primary efficacy analysis data cut-off date, including cases confirmed by the central laboratory and cases with documented positive SARS-CoV-2 PCR from a local laboratory which are still awaiting confirmation by the central laboratory, were included. The concordance rate observed up to the data cut-off date between the PCR results from the local laboratory and the central laboratory was 90.3%.

Table 12: Summary of Vaccine Efficacy against Moderate to Severe/Critical and Severe/Critical COVID-19 for Countries With >100 Reported Moderate to Severe/Critical Cases

		Severity	
	Onset	**Moderate to Severe/Critical Point estimate (95% CI)**	**Severe/Critical Point estimate (95% CI)**
US	at least **14 days** after vaccination	74.4% (65.0; 81.6)	78.0% (33.1; 94.6)
	at least **28 days** after vaccination	72.0% (58.2;81.7)	85.9% (-9.4; 99.7)
Brazil	at least **14 days** after vaccination	66.2% (51.0; 77.1)	81.9% (17.0; 98.1)
	at least **28 days** after vaccination	68.1% (48.8; 80.7)	87.6% (7.8; 99.7)
South Africa	at least **14 days** after vaccination	52.0% (30.3; 67.4)	73.1% (40.0; 89.4)
	at least **28 days** after vaccination	64.0% (41.2; 78.7)	81.7% (46.2; 95.4)

Strain sequencing was conducted on available samples with sufficient viral load from centrally confirmed COVID-19 cases (one sequence per case). As of February 12, 2021, samples from 71.7% of central laboratory confirmed primary analysis cases had been sequenced [United States (73.5%), South Africa (66.9%) and Brazil (69.3%)]. In the United States, 96.4% of strains were identified as the Wuhan-H1 variant D614G; in South Africa, 94.5% of strains were identified as the 20H/501Y.V2 variant (B.1.351 lineage); in Brazil, 69.4% of strains were identified to be a variant of the P.2 lineage and 30.6% of strains were identified as the Wuhan-H1 variant D614G. As of February 12, 2021, SARS-CoV-2 variants from the B1.1.7 or P.1 lineages were not found in any of the sequenced samples.

18.2 Immunogenicity of a Booster Dose following Primary Vaccination with Janssen COVID-19 Vaccine

In Study 2, individuals 18 through 55 years of age and 65 years and older received a booster dose of the Janssen COVID-19 Vaccine approximately 2 months after the primary vaccination. Immunogenicity was assessed by measuring neutralizing antibodies to SARS-CoV-2 Victoria/1/2020 strain using a qualified wild-type virus neutralization assay (wtVNA). Immunogenicity data are available from 39 individuals, of whom 15 were 65 years of age and older, and are summarized in Table 13. Based on a limited number of individuals from this study, a similar fold-rise in neutralizing antibody titers from pre-booster to 14 and 28 days post-booster

was observed between individuals 18 through 55 years of age and individuals 65 years of age and older.

Table 13. Study 2 - SARS-CoV-2 Neutralization Wild Type VNA-VICTORIA/1/2020 (IC50), , Per Protocol Immunogenicity Set*

	Baseline (Day 1)	28 Days Post-Primary Vaccination (Day 29)	Pre-Booster Dose (Day 57)	14 Days Post-Booster Dose (Day 71)	28 Days Post-Booster Dose (Day 85)
N	38	39	39	39	38
Geometric mean titer (95% CI)	<LLOQ (<LLOQ, <LLOQ)	260 (196, 346)	212 (142, 314)	518 (354, 758)	424 (301, 597)
Geometric mean fold increase (95% CI) from baseline	n/a	4.4 (3.3, 5.7)	3.7 (2.6, 5.2)	8.8 (6.1, 12.8)	7.4 (5.4, 10.2)
Geometric mean fold increase (95% CI) from day 29	n/a	n/a	0.9 (0.7; 1.1)	2.0 (1.5; 2.7)	1.6 (1.2; 2.1)
Geometric mean fold increase (95% CI) from pre-booster	n/a	n/a	n/a	2.3 (1.7, 3.1)	1.8 (1.4, 2.4)

LLOQ = lower limit of quantification

* PPI set: The per protocol immunogenicity population includes all randomized and vaccinated participants for whom immunogenicity data are available excluding participants with major protocol deviations expected to impact the immunogenicity outcomes. In addition, samples obtained after missed vaccinations or participants with SARS-CoV-2 infection occurring after screening were excluded from the analysis.

18.3 Immunogenicity of a Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

Effectiveness of a Janssen COVID-19 Vaccine booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 Vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Janssen COVID-19 Vaccine booster dose administered following completion of Janssen COVID-19 Vaccine primary vaccination and from immunogenicity data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the Janssen COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Janssen COVID-19 Vaccine was demonstrated regardless of primary vaccination.

19 HOW SUPPLIED/STORAGE AND HANDLING

Janssen COVID-19 Vaccine is supplied in a carton of 10 multi-dose vials (NDC 59676-580-15). A maximum of 5 doses can be withdrawn from the multi-dose vial.

The storage and handling information in this Fact Sheet supersedes the storage and handling information on the carton and vial labels.

Storage Prior to First Puncture of the Vaccine Vial

Store unpunctured multi-dose vials of the Janssen COVID-19 Vaccine at 2°C to 8°C (36°F to 46°F) and protect from light. Do not store frozen.

Unpunctured vials of Janssen COVID-19 Vaccine may be stored between 9°C to 25°C (47°F to 77°F) for up to 12 hours.

The Janssen COVID-19 Vaccine is initially stored frozen by the manufacturer, then shipped at 2°C to 8°C (36°F to 46°F). If vaccine is still frozen upon receipt, thaw at 2°C to 8°C (36°F to 46°F). If needed immediately, thaw at room temperature (maximally 25°C/77°F). At room temperature (maximally 25°C/77°F), a carton of 10 vials will take approximately 4 hours to thaw, and an individual vial will take approximately 1 hour to thaw. Do not refreeze once thawed.

Storage After First Puncture of the Vaccine Vial

After the first dose has been withdrawn, hold the vial between 2° to 8°C (36° to 46°F) for up to 6 hours or at room temperature (maximally 25°C/77°F) for up to 2 hours. Discard the vial if vaccine is not used within these times.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at:
https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions or to access the most recent Janssen COVID-19 Vaccine Fact Sheets, scan the QR code using your device, visit www.janssencovid19vaccine.com or call the telephone numbers provided below.

QR Code	Fact Sheets Website	Telephone numbers
	www.janssencovid19vaccine.com.	US Toll Free: 1-800-565-4008 US Toll: 1-908-455-9922

This Full EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please see www.janssencovid19vaccine.com.

Manufactured by:
Janssen Biotech, Inc.
a Janssen Pharmaceutical Company of Johnson & Johnson
Horsham, PA 19044, USA

Revised: Oct/20/2021

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE MODERNA COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, **MODERNA COVID-19 VACCINE**, for active immunization to prevent COVID-19 in individuals 18 years of age and older.

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS
Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults, and cases of COVID-19 that result in hospitalization or death following administration of the Moderna COVID-19 Vaccine. See "MANDATORY REQUIREMENTS FOR MODERNA COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

The Moderna COVID-19 Vaccine is a suspension for intramuscular injection.

Primary Series:
Each primary series dose of the Moderna COVID-19 Vaccine is **0.5 mL**.

The Moderna COVID-19 Vaccine is administered as a primary series of two doses (0.5 mL each) 1 month apart to individuals 18 years of age or older.

A third primary series dose of the Moderna COVID-19 Vaccine (0.5 mL) at least 1 month following the second dose is authorized for administration to individuals at least 18 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose:
The booster dose of the Moderna COVID-19 Vaccine is **0.25 mL**.

A single Moderna COVID-19 Vaccine booster dose (0.25 mL) may be administered intramuscularly at least 6 months after completing a primary series of the Moderna COVID-19 Vaccine to individuals:

- 65 years of age and older
- 18 through 64 years of age at high risk of severe COVID-19
- 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2

A single booster dose of the Moderna COVID-19 Vaccine (0.25 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the

heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.modernatx.com/covid19vaccine-eua.

For information on clinical trials that are testing the use of the Moderna COVID-19 Vaccine for active immunization against COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle and body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

Storage and Handling

The information in this Fact Sheet supersedes the information on the vial and carton labels.

During storage, minimize exposure to room light.

The Moderna COVID-19 Vaccine multiple-dose vials are stored frozen between -50º to -15ºC (-58º to 5ºF). Store in the original carton to protect from light.

Do not store on dry ice or below -50ºC (-58ºF). Use of dry ice may subject vials to temperatures colder than -50°C (-58°F).

Vials may be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use.

Vials may be stored between 8° to 25°C (46° to 77°F) for a total of 24 hours.

After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Vials should be discarded 12 hours after the first puncture.

Thawed vials can be handled in room light conditions.

Do not refreeze once thawed.

Transportation of Thawed Vials at 2° to 8°C (36° to 46°F)

If transport at -50° to -15°C (-58° to 5°F) is not feasible, available data support transportation of one or more thawed vials for up to 12 hours at 2° to 8°C (36° to 46°F) when shipped using shipping containers which have been qualified to maintain 2° to 8°C (36° to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. Once thawed and transported at 2° to 8°C (36° to 46°F), vials should not be refrozen and should be stored at 2° to 8°C (36° to 46°F) until use.

Dosing and Schedule

Primary Series:
Each primary series dose of the Moderna COVID-19 Vaccine is **0.5 mL**.

The Moderna COVID-19 Vaccine is administered as a primary series of two doses (0.5 mL each) 1 month apart to individuals 18 years of age or older.

A third primary series dose of the Moderna COVID-19 Vaccine (0.5 mL) at least 1 month following the second dose is authorized for administration to individuals at least 18 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose:
The booster dose of the Moderna COVID-19 Vaccine is **0.25 mL**.

A single Moderna COVID-19 Vaccine booster dose (0.25 mL) may be administered intramuscularly at least 6 months after completing a primary series of the Moderna COVID-19 Vaccine to individuals:

- 65 years of age and older
- 18 through 64 years of age at high risk of severe COVID-19
- 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2

A single booster dose of the Moderna COVID-19 Vaccine (0.25 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

Dose Preparation

- The Moderna COVID-19 Vaccine multiple-dose vials contain a frozen suspension that does not contain a preservative and must be thawed prior to administration.
- Remove the required number of vial(s) from storage and thaw each vial before use following the instructions below.

Multiple-dose Vials Containing	Thaw in Refrigerator	Thaw at Room Temperature
5.5 mL	Thaw in refrigerated conditions between 2° to 8°C (36° to 46°F) for 2 hours and 30 minutes. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C (59° to 77°F) for 1 hour.
7.5 mL	Thaw in refrigerated conditions between 2° to 8°C (36° to 46°F) for 3 hours. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C (59° to 77°F) for 1 hour and 30 minutes.

- After thawing, do not refreeze.
- Swirl vial gently after thawing and between each withdrawal. **Do not shake.** Do not dilute the vaccine.
- The Moderna COVID-19 Vaccine is a white to off-white suspension. It may contain white or translucent product-related particulates. Visually inspect the Moderna COVID-19 Vaccine vials for other particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.
- The Moderna COVID-19 Vaccine is supplied in two multiple-dose vial presentations:
  - A multiple-dose vial containing 5.5 mL
  - A multiple-dose vial containing 7.5 mL
- Primary series doses of 0.5 mL and booster doses of 0.25 mL may be extracted from either vial presentation, preferentially using low dead-volume syringes and/or needles.
- When extracting only primary series doses, depending on the syringes and needles used, a maximum of 11 doses (range: 10-11 doses) may be extracted from the vial containing 5.5 mL or a maximum of 15 doses (range: 13-15 doses) may be extracted from the vial containing 7.5 mL.
- When extracting only booster doses or a combination of primary series and booster doses, the maximum number of doses that may be extracted from either vial presentation should not exceed 20 doses. Do not puncture the vial stopper more than 20 times.
- Irrespective of the type of syringe and needle:
  - Each primary series dose must contain 0.5 mL of vaccine.
  - Each booster dose must contain 0.25 mL of vaccine.
  - If the vial stopper has been punctured 20 times, discard the vial and contents.
  - If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL or 0.25 mL, discard the vial and contents. Do not pool excess vaccine from multiple vials.
- After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Record the date and time of first use on the Moderna COVID-19 Vaccine vial label. Discard vial after 12 hours. Do not refreeze.

Administration
Visually inspect each dose of the Moderna COVID-19 Vaccine in the dosing syringe prior to administration. The white to off-white suspension may contain white or translucent product-related particulates. During the visual inspection,

- verify the final dosing volume of 0.5 mL for a primary series dose or 0.25 mL for a booster dose.
- confirm there are no other particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains other particulate matter.

Administer the Moderna COVID-19 Vaccine intramuscularly.

CONTRAINDICATION
Do not administer the Moderna COVID-19 Vaccine to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Moderna COVID-19 Vaccine *(see Full EUA Prescribing Information)*.

WARNINGS

Management of Acute Allergic Reactions
Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Moderna COVID-19 Vaccine.

Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Myocarditis and Pericarditis
Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 18 through 24 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

Syncope
Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

Altered Immunocompetence
Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Moderna COVID-19 Vaccine.

Limitations of Vaccine Effectiveness
The Moderna COVID-19 Vaccine may not protect all vaccine recipients.

ADVERSE REACTIONS

Adverse Reactions in Clinical Trials
Adverse reactions reported in clinical trials following administration of the Moderna COVID-19 Vaccine include pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, axillary swelling/tenderness, fever, swelling at the injection site, erythema at the injection site, and rash. *(See Full EUA Prescribing Information)*

Adverse Reactions in Post-Authorization Experience
Anaphylaxis and other severe allergic reactions, myocarditis, pericarditis, and syncope have been reported following administration of the Moderna COVID-19 Vaccine during mass vaccination outside of clinical trials.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Moderna COVID-19 Vaccine.

USE WITH OTHER VACCINES

There is no information on the co-administration of the Moderna COVID-19 Vaccine with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.modernatx.com/covid19vaccine-eua to obtain the Fact Sheet) prior to the individual receiving each dose of the Moderna COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Moderna COVID-19 Vaccine, which is not an FDA-approved vaccine.
- The recipient or their caregiver has the option to accept or refuse the Moderna COVID-19 Vaccine.
- The significant known and potential risks and benefits of the Moderna COVID-19 Vaccine, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are evaluating the use of the Moderna COVID-19 Vaccine to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of Moderna COVID-19 Vaccine.

Provide the **v-safe** information sheet to vaccine recipients/caregivers and encourage vaccine

recipients to participate in **v-safe**. **V-safe** is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. **V-safe** asks questions that help CDC monitor the safety of COVID-19 vaccines. **V-safe** also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR MODERNA COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of the Moderna COVID-19 Vaccine, the following items are required. Use of unapproved Moderna COVID-19 Vaccine for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. The Moderna COVID-19 Vaccine is authorized for use in individuals 18 years of age and older.

2. The vaccination provider must communicate to the individual receiving the Moderna COVID-19 Vaccine or their caregiver information consistent with the “Fact Sheet for Recipients and Caregivers” prior to the individual receiving the Moderna COVID-19 Vaccine.

3. The vaccination provider must include vaccination information in the state/local jurisdiction’s Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):
   - vaccine administration errors whether or not associated with an adverse event,
   - serious adverse events* (irrespective of attribution to vaccination),
   - cases of Multisystem Inflammatory Syndrome (MIS) in adults, and
   - cases of COVID-19 that result in hospitalization or death.

   Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS, call 1-800-822-7967. The reports should include the words “Moderna COVID-19 Vaccine EUA” in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of MIS in adults, and cases of COVID-19 that result in hospitalization or death following administration of the Moderna COVID-19 Vaccine to recipients.

   *Serious adverse events are defined as:
   - Death;
   - A life-threatening adverse event;

- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND MODERNATX, INC.
Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to ModernaTX, Inc. using the contact information below or by providing a copy of the VAERS form to ModernaTX, Inc.

Email	Fax number	Telephone number
ModernaPV@modernatx.com	1-866-599-1342	1-866-MODERNA (1-866-663-3762)

ADDITIONAL INFORMATION
For general questions, visit the website or call the telephone number provided below.

To access the most recent Moderna COVID-19 Vaccine Fact Sheets, please scan the QR code or visit the website provided below.

Website	Telephone number
www.modernatx.com/covid19vaccine-eua	1-866-MODERNA (1-866-663-3762)

AVAILABLE ALTERNATIVES
Comirnaty (COVID-19 Vaccine, mRNA) is an FDA-approved vaccine to prevent COVID-19 caused by SARS-CoV-2. There may be clinical trials or availability under EUA of other COVID-19 vaccines.

FEDERAL COVID-19 VACCINATION PROGRAM
This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any

out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, HRSA COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 Pandemic. In response, the FDA has issued an EUA for the unapproved product, Moderna COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 18 years of age and older.

FDA issued this EUA, based on ModernaTX, Inc.'s request and submitted data.

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Moderna COVID-19 Vaccine may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Moderna COVID-19 Vaccine will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization, visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

COUNTERMEASURES INJURY COMPENSATION PROGRAM

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the vaccines to prevent COVID-19, visit http://www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Moderna US, Inc.
Cambridge, MA 02139

Patent(s): www.modernatx.com/patents
Revised: Oct/20/2021

END SHORT VERSION FACT SHEET
Long Version (Full EUA Prescribing Information) Begins On Next Page

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

MODERNA COVID-19 VACCINE

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

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FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

Moderna COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

- The Moderna COVID-19 Vaccine multiple-dose vials contain a frozen suspension that does not contain a preservative and must be thawed prior to administration.
- Remove the required number of vial(s) from storage and thaw each vial before use following the instructions below.

Multiple-dose Vials Containing	Thaw in Refrigerator	Thaw at Room Temperature
5.5 mL	Thaw in refrigerated conditions between 2° to 8°C (36° to 46°F) for 2 hours and 30 minutes. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C (59° to 77°F) for 1 hour.
7.5 mL	Thaw in refrigerated conditions between 2° to 8°C (36° to 46°F) for 3 hours. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw at room temperature between 15° to 25°C (59° to 77°F) for 1 hour and 30 minutes.

- After thawing, do not refreeze.
- Swirl vial gently after thawing and between each withdrawal. **Do not shake.** Do not dilute the vaccine.
- The Moderna COVID-19 Vaccine is a white to off-white suspension. It may contain white or translucent product-related particulates. Visually inspect the Moderna COVID-19 Vaccine vials for other particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.
- The Moderna COVID-19 Vaccine is supplied in two multiple-dose vial presentations:
    - A multiple-dose vial containing 5.5 mL
    - A multiple-dose vial containing 7.5 mL
- Primary series doses of 0.5 mL and booster doses of 0.25 mL may be extracted from either vial presentation, preferentially using low dead-volume syringes and/or needles.
- When extracting only primary series doses, depending on the syringes and needles used, a maximum of 11 doses (range: 10-11 doses) may be extracted from the vial containing 5.5 mL or a maximum of 15 doses (range: 13-15 doses) may be extracted from the vial containing 7.5 mL.
- When extracting only booster doses or a combination of primary series and booster doses, the maximum number of doses that may be extracted from either vial presentation should not exceed 20 doses. Do not puncture the vial stopper more than 20 times.
- Irrespective of the type of syringe and needle:
    - Each primary series dose must contain 0.5 mL of vaccine.
    - Each booster dose must contain 0.25 mL of vaccine.
    - If the vial stopper has been punctured 20 times, discard the vial and contents.
    - If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL or 0.25 mL, discard the vial and contents. Do not pool excess vaccine from multiple vials.
- After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Record the date and time of first use on the Moderna COVID-19 Vaccine vial label. Discard vial after 12 hours. Do not refreeze.

2.2 Administration

Visually inspect each dose of the Moderna COVID-19 Vaccine in the dosing syringe prior to administration. The white to off-white suspension may contain white or translucent product-related particulates. During the visual inspection,

- verify the final dosing volume of 0.5 mL for a primary series dose or 0.25 mL for a booster dose.
- confirm there are no other particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains other particulate matter.

Administer the Moderna COVID-19 Vaccine intramuscularly.

2.3 Dosing and Schedule

Primary Series:
Each primary series dose of the Moderna COVID-19 Vaccine is **0.5 mL**.

The Moderna COVID-19 Vaccine is administered as a primary series of two doses (0.5 mL each) 1 month apart to individuals 18 years of age or older.

A third primary series dose of the Moderna COVID-19 Vaccine (0.5 mL) at least 1 month following the second dose is authorized for administration to individuals at least 18 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose:
The booster dose of the Moderna COVID-19 Vaccine is **0.25 mL**.

A single Moderna COVID-19 Vaccine booster dose (0.25 mL) may be administered intramuscularly at least 6 months after completing a primary series of the Moderna COVID-19 Vaccine to individuals:

- 65 years of age and older
- 18 through 64 years of age at high risk of severe COVID-19
- 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2

A single booster dose of the Moderna COVID-19 Vaccine (0.25 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

3 DOSAGE FORMS AND STRENGTHS

Moderna COVID-19 Vaccine is a suspension for intramuscular injection.

- Each primary series dose is 0.5 mL.
- The booster dose is 0.25 mL.

4 CONTRAINDICATIONS

Do not administer the Moderna COVID-19 Vaccine to individuals with a known history of severe allergic reaction (e.g., anaphylaxis) to any component of the Moderna COVID-19 Vaccine *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the Moderna COVID-19 Vaccine.

Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 18 through 24 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished response to the Moderna COVID-19 Vaccine.

5.5 Limitations of Vaccine Effectiveness

The Moderna COVID-19 Vaccine may not protect all vaccine recipients.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults, and hospitalized or fatal cases of COVID-19 following vaccination with the Moderna COVID-19 Vaccine. To the extent feasible, provide a copy of the VAERS form to ModernaTX, Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and ModernaTX, Inc.

In a clinical study, the adverse reactions in participants 18 years of age and older following administration of the primary series included pain at the injection site (92.0%), fatigue (70.0%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23.0%), axillary swelling/tenderness (19.8%), fever (15.5%), swelling at the injection site (14.7%), and erythema at the injection site (10.0%).

In a clinical study, the adverse reactions in participants 18 years of age and older following administration of a booster dose included pain at the injection site (83.8%), fatigue (58.7%), headache (55.1%), myalgia (49.1%), arthralgia (41.3%), chills (35.3%), axillary swelling/tenderness (20.4%), nausea/vomiting (11.4%), fever (6.6%), swelling at the injection site (5.4%), and erythema at the injection site (4.8%), rash (1.8%).

Anaphylaxis and other severe allergic reactions, myocarditis, pericarditis, and syncope have been reported following administration of the Moderna COVID-19 Vaccine outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Overall, 15,419 participants aged 18 years and older received at least one dose of Moderna COVID-19 Vaccine in three clinical trials (NCT04283461, NCT04405076, and NCT04470427). In a fourth clinical trial (NCT04885907), 60 solid organ transplant recipients received a third dose of Moderna COVID-19 Vaccine.

Two-Dose Primary Series

The safety of Moderna COVID-19 Vaccine was evaluated in an ongoing Phase 3 randomized, placebo-controlled, observer-blind clinical trial conducted in the United States involving 30,351 participants 18 years of age and older who received at least one dose (0.5 mL) of Moderna COVID-19 Vaccine (n=15,185) or placebo (n=15,166) (Study 1, NCT04470427). At the time of

vaccination, the mean age of the population was 52 years (range 18-95); 22,831 (75.2%) of participants were 18 to 64 years of age and 7,520 (24.8%) of participants were 65 years of age and older. Overall, 52.7% were male, 47.3% were female, 20.5% were Hispanic or Latino, 79.2% were White, 10.2% were African American, 4.6% were Asian, 0.8% were American Indian or Alaska Native, 0.2% were Native Hawaiian or Pacific Islander, 2.1% were other races, and 2.1% were Multiracial. Demographic characteristics were similar among participants who received Moderna COVID-19 Vaccine and those who received placebo.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among participants receiving Moderna COVID-19 Vaccine (n=15,179) and participants receiving placebo (n=15,163) with at least 1 documented dose. Events that persisted for more than 7 days were followed until resolution. Solicited adverse reactions were reported more frequently among vaccine participants than placebo participants.

The reported number and percentage of the solicited local and systemic adverse reactions by age group and dose are presented in Table 1 and Table 2, respectively.

Table 1: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 18-64 Years (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		**Placebo[a]**	
	Dose 1 (N=11,406) n (%)	**Dose 2** (N=10,985) n (%)	**Dose 1** (N=11,407) n (%)	**Dose 2** (N=10,918) n (%)
Local Adverse Reactions				
Pain	9,908 (86.9)	9,873 (89.9)	2,177 (19.1)	2,040 (18.7)
Pain, Grade 3[b]	366 (3.2)	506 (4.6)	23 (0.2)	22 (0.2)
Axillary swelling/tenderness	1,322 (11.6)	1,775 (16.2)	567 (5.0)	470 (4.3)
Axillary swelling/tenderness, Grade 3[b]	37 (0.3)	46 (0.4)	13 (0.1)	11 (0.1)
Swelling (hardness) ≥25 mm	767 (6.7)	1,389 (12.6)	34 (0.3)	36 (0.3)
Swelling (hardness), Grade 3[c]	62 (0.5)	182 (1.7)	3 (<0.1)	4 (<0.1)
Erythema (redness) ≥25 mm	344 (3.0)	982 (8.9)	47 (0.4)	43 (0.4)
Erythema (redness), Grade 3[c]	34 (0.3)	210 (1.9)	11 (<0.1)	12 (0.1)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=11,406) n (%)	**Dose 2** (N=10,985) n (%)	**Dose 1** (N=11,407) n (%)	**Dose 2** (N=10,918) n (%)
Systemic Adverse Reactions				
Fatigue	4,384 (38.4)	7,430 (67.6)	3,282 (28.8)	2,687 (24.6)
Fatigue, Grade 3[d]	120 (1.1)	1,174 (10.7)	83 (0.7)	86 (0.8)
Fatigue, Grade 4[e]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache	4,030 (35.3)	6,898 (62.8)	3,304 (29.0)	2,760 (25.3)
Headache, Grade 3[f]	219 (1.9)	553 (5.0)	162 (1.4)	129 (1.2)
Myalgia	2,699 (23.7)	6,769 (61.6)	1,628 (14.3)	1,411 (12.9)
Myalgia, Grade 3[d]	73 (0.6)	1,113 (10.1)	38 (0.3)	42 (0.4)
Arthralgia	1,893 (16.6)	4,993 (45.5)	1,327 (11.6)	1,172 (10.7)
Arthralgia, Grade 3[d]	47 (0.4)	647 (5.9)	29 (0.3)	37 (0.3)
Arthralgia, Grade 4[e]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills	1,051 (9.2)	5,341 (48.6)	730 (6.4)	658 (6.0)
Chills, Grade 3[g]	17 (0.1)	164 (1.5)	8 (<0.1)	15 (0.1)
Nausea/vomiting	1,068 (9.4)	2,348 (21.4)	908 (8.0)	801 (7.3)
Nausea/vomiting, Grade 3[h]	6 (<0.1)	10 (<0.1)	8 (<0.1)	8 (<0.1)
Fever	105 (0.9)	1,908 (17.4)	37 (0.3)	39 (0.4)
Fever, Grade 3[i]	10 (<0.1)	184 (1.7)	1 (<0.1)	2 (<0.1)
Fever, Grade 4[j]	4 (<0.1)	12 (0.1)	4 (<0.1)	2 (<0.1)
Use of antipyretic or pain medication	2,656 (23.3)	6,292 (57.3)	1,523 (13.4)	1,248 (11.4)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
[d] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.
[f] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[g] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

[h] Grade 3 nausea/vomiting: Defined as prevents daily activity; requires outpatient intravenous hydration.
[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Table 2: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 65 Years and Older (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,762) n (%)	**Dose 2** (N=3,692) n (%)	**Dose 1** (N=3,748) n (%)	**Dose 2** (N=3,648) n (%)
Local Adverse Reactions				
Pain	2,782 (74.0)	3,070 (83.2)	481 (12.8)	437 (12.0)
Pain, Grade 3[b]	50 (1.3)	98 (2.7)	32 (0.9)	18 (0.5)
Axillary swelling/tenderness	231 (6.1)	315 (8.5)	155 (4.1)	97 (2.7)
Axillary swelling/tenderness, Grade 3[b]	12 (0.3)	21 (0.6)	14 (0.4)	8 (0.2)
Swelling (hardness) ≥25 mm	165 (4.4)	400 (10.8)	18 (0.5)	13 (0.4)
Swelling (hardness), Grade 3[c]	20 (0.5)	72 (2.0)	3 (<0.1)	7 (0.2)
Erythema (redness) ≥25 mm	86 (2.3)	275 (7.5)	20 (0.5)	13 (0.4)
Erythema (redness), Grade 3[c]	8 (0.2)	77 (2.1)	2 (<0.1)	3 (<0.1)
Systemic Adverse Reactions				
Fatigue	1,251 (33.3)	2,152 (58.3)	851 (22.7)	716 (19.6)
Fatigue, Grade 3[d]	30 (0.8)	254 (6.9)	22 (0.6)	20 (0.5)
Headache	921 (24.5)	1,704 (46.2)	723 (19.3)	650 (17.8)
Headache, Grade 3[e]	52 (1.4)	106 (2.9)	34 (0.9)	33 (0.9)
Myalgia	742 (19.7)	1,739 (47.1)	443 (11.8)	398 (10.9)
Myalgia, Grade 3[d]	17 (0.5)	205 (5.6)	9 (0.2)	10 (0.3)
Arthralgia	618 (16.4)	1,291 (35.0)	456 (12.2)	397 (10.9)
Arthralgia, Grade 3[d]	13 (0.3)	123 (3.3)	8 (0.2)	7 (0.2)
Chills	202 (5.4)	1,141 (30.9)	148 (4.0)	151 (4.1)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,762) n (%)	**Dose 2** (N=3,692) n (%)	**Dose 1** (N=3,748) n (%)	**Dose 2** (N=3,648) n (%)
Chills, Grade 3[f]	7 (0.2)	27 (0.7)	6 (0.2)	2 (<0.1)
Nausea/vomiting	194 (5.2)	437 (11.8)	166 (4.4)	133 (3.6)
Nausea/vomiting, Grade 3[g]	4 (0.1)	10 (0.3)	4 (0.1)	3 (<0.1)
Nausea/vomiting, Grade 4[h]	0 (0)	1 (<0.1)	0 (0)	0 (0)
Fever	10 (0.3)	370 (10.0)	7 (0.2)	4 (0.1)
Fever, Grade 3[i]	1 (<0.1)	18 (0.5)	1 (<0.1)	0 (0)
Fever, Grade 4[j]	0 (0)	1 (<0.1)	2 (<0.1)	1 (<0.1)
Use of antipyretic or pain medication	673 (17.9)	1,546 (41.9)	477 (12.7)	329 (9.0)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
[a] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
[d] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[f] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[g] Grade 3 nausea/vomiting: Defined as prevents daily activity; requires outpatient intravenous hydration.
[h] Grade 4 nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Solicited local and systemic adverse reactions reported following administration of Moderna COVID-19 Vaccine had a median duration of 1 to 3 days.

Grade 3 solicited local adverse reactions were more frequently reported after Dose 2 than after Dose 1. Solicited systemic adverse reactions were more frequently reported by vaccine recipients after Dose 2 than after Dose 1.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following each dose and follow-up is ongoing. Serious adverse events and medically attended adverse events will be recorded for the entire study duration of 2 years. As of November 25, 2020, among participants who had received at least 1 dose of vaccine or placebo (vaccine=15,185, placebo=15,166), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 23.9% of participants (n=3,632) who received Moderna COVID-19 Vaccine and 21.6% of

participants (n=3,277) who received placebo. In these analyses, 87.9% of study participants had at least 28 days of follow-up after Dose 2.

Lymphadenopathy-related events that were not necessarily captured in the 7-day e-diary were reported by 1.1% of vaccine recipients and 0.6% of placebo recipients. These events included lymphadenopathy, lymphadenitis, lymph node pain, vaccination-site lymphadenopathy, injection-site lymphadenopathy, and axillary mass, which were plausibly related to vaccination. This imbalance is consistent with the imbalance observed for solicited axillary swelling/tenderness in the injected arm.

Hypersensitivity adverse events were reported in 1.5% of vaccine recipients and 1.1% of placebo recipients. Hypersensitivity events in the vaccine group included injection site rash and injection site urticaria, which are likely related to vaccination. Delayed injection site reactions that began >7 days after vaccination were reported in 1.2% of vaccine recipients and 0.4% of placebo recipients. Delayed injection site reactions included pain, erythema, and swelling and are likely related to vaccination.

Throughout the same period, there were three reports of Bell's palsy in the Moderna COVID-19 Vaccine group (one of which was a serious adverse event), which occurred 22, 28, and 32 days after vaccination, and one in the placebo group which occurred 17 days after vaccination. Currently available information on Bell's palsy is insufficient to determine a causal relationship with the vaccine.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

As of November 25, 2020, serious adverse events were reported by 1.0% (n=147) of participants who received Moderna COVID-19 Vaccine and 1.0% (n=153) of participants who received placebo, one of which was the case of Bell's palsy which occurred 32 days following receipt of vaccine.

In these analyses, 87.9% of study participants had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 9 weeks after Dose 2.

There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported 1 and 2 days, respectively, after vaccination and was likely related to vaccination.

There was one serious adverse event of intractable nausea and vomiting in a participant with prior history of severe headache and nausea requiring hospitalization. This event occurred 1 day after vaccination and was likely related to vaccination.

There were no other notable patterns or imbalances between treatment groups for specific

categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Solid Organ Transplant Recipients

From an independent study (NCT04885907), in 60 participants who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years previously (range 1.99-6.75 years) who received a third vaccine dose (0.5 mL), the adverse event profile was similar to that after the second dose and no Grade 3 or Grade 4 events were reported.

Booster Dose Following a Primary Series of Moderna COVID-19 Vaccine

Study 2 is an ongoing Phase 2, randomized, observer-blind, placebo-controlled, dose-confirmation study to evaluate the safety, reactogenicity, and immunogenicity of the Moderna COVID-19 Vaccine in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL 1 month apart) of the Moderna COVID-19 Vaccine primary series. In an open label-phase, 171 of those participants received a single booster dose (0.25 mL) at least 6 months (range of 5.8 to 8.5 months) after receiving the second dose of the primary series. Safety monitoring after the booster dose was the same as that described for Study 1 participants who received the primary series.

Among the 171 booster dose recipients, the median age was 55 years (range 18-87), 39.2% were male and 60.8% were female, 95.9% were White, 5.8% were Hispanic or Latino, 2.9% were Black or African American, 0.6% were Asian, and 0.6% were American Indian or Alaska Native. Following the booster dose, the median follow-up time was 5.7 months (range of 3.1 to 6.4 months).

Solicited Adverse Reactions

Tables 3 and 4 present the frequency and severity of reported solicited local and systemic adverse reactions among Study 2 Moderna COVID-19 Vaccine booster dose recipients 18 to <65 years of age and ≥65 years of age, respectively, within 7 days of a booster vaccination.

Table 3: Number and Percentage of Study 2 Participants 18-64 Years of Age With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After the Booster Dose or After the Second Dose of Primary Series (Solicited Safety Set)

	Study 2 Second Dose of Primary Series (N=155) n (%)	**Study 2 Booster Dose** (N=129) n (%)
Local Adverse Reactions		
Pain	137 (88.4)	111 (86.0)
Pain, Grade 3[a]	1 (0.6)	4 (3.1)
Axillary swelling/tenderness	18 (11.6)	32 (24.8)

	Study 2 Second Dose of Primary Series (N=155) n (%)	Study 2 Booster Dose (N=129) n (%)
Axillary swelling/tenderness, Grade 3[a]	0 (0)	1 (0.8)
Swelling (hardness) ≥25 mm	16 (10.3)	8 (6.2)
Erythema (redness) ≥25 mm	12 (7.7)	7 (5.4)
Erythema (redness), Grade 3[b]	2 (1.3)	1 (0.8)
Systemic Adverse Reactions		
Fatigue	105 (67.7)	80 (62.0)
Fatigue, Grade 3[c]	16 (10.3)	4 (3.1)
Headache	87 (56.1)	76 (58.9)
Headache, Grade 3[d]	8 (5.2)	1 (0.8)
Myalgia	89 (57.4)	64 (49.6)
Myalgia, Grade 3[c]	15 (9.7)	4 (3.1)
Arthralgia	66 (42.6)	54 (41.9)
Arthralgia, Grade 3[c]	8 (5.2)	4 (3.1)
Chills	71 (45.8)	52 (40.3)
Chills, Grade 3[e]	1 (0.6)	0 (0)
Nausea/vomiting	36 (23.2)	16 (12.4)
Fever	24 (15.5)	9 (7.0)
Fever, Grade 3[f]	3 (1.9)	2 (1.6)
Rash	5 (3.2)	3 (2.3)
Use of antipyretic or pain medication	86 (55.5)	64 (49.6)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
[a] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[b] Grade 3 erythema: Defined as >100 mm / >10 cm.
[c] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[d] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[e] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[f] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.

Table 4: Number and Percentage of Study 2 Participants ≥65 Years of Age With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After the Booster Dose or After the Second Dose of Primary Series (Solicited Safety Set)

	Study 2 Second Dose of Primary Series (N=43) n (%)	Study 2 Booster Dose (N=38) n (%)
Local Adverse Reactions		
Pain	32 (74.4)	29 (76.3)
Pain, Grade 3[a]	0 (0.0)	2 (5.3)
Axillary swelling/tenderness	2 (4.7)	2 (5.3)
Swelling (hardness) ≥25 mm	5 (11.6)	1 (2.6)
Swelling (hardness), Grade 3[b]	1 (2.3)	1 (2.6)
Erythema (redness) ≥25 mm	3 (7.0)	1 (2.6)
Erythema (redness), Grade 3[b]	3 (7.0)	0 (0.0)

	Study 2 Second Dose of Primary Series (N=43) n (%)	Study 2 Booster Dose (N=38) n (%)
Systemic Adverse Reactions		
Fatigue	23 (53.5)	18 (47.4)
Fatigue, Grade 3[c]	2 (4.7)	3 (7.9)
Myalgia	15 (34.9)	18 (47.4)
Myalgia, Grade 3[c]	0 (0)	1 (2.6)
Headache	17 (39.5)	16 (42.1)
Headache, Grade 3[d]	1 (2.3)	1 (2.6)
Arthralgia	11 (25.6)	15 (39.5)
Arthralgia, Grade 3[c]	0 (0)	1 (2.6)
Chills	7 (16.3)	7 (18.4)
Nausea/vomiting	5 (11.6)	3 (7.9)
Fever	2 (4.7)	2 (5.4)
Fever, Grade 3[e]	1 (2.3)	0 (0)
Rash	1 (2.3)	0 (0.0)
Use of antipyretic or pain medication	11 (25.6)	11 (28.9)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
a Grade 3 pain: Defined as any use of prescription pain reliever; prevents daily activity.
b Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
c Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
d Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
e Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.

In participants who received a booster dose, the median duration of solicited local and systemic adverse reactions was 2 to 3 days.

Unsolicited Adverse Events

Overall, the 171 participants who received a booster dose, had a median follow-up time of 5.7 months after the booster dose to the cut-off date (August 16, 2021). Through the cut-off date, there were no unsolicited adverse events not already captured as solicited local and systemic reactions that were considered causally related to the Moderna COVID-19 Vaccine.

Serious Adverse Events

Of the 171 participants who received a booster dose of Moderna COVID-19 Vaccine, there were no serious adverse events reported from the booster dose through 28 days after the booster dose. Through the cut-off date of August 16, 2021, there were no serious adverse events following the booster dose considered causally related to the Moderna COVID-19 Vaccine.

Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

The safety of a Moderna COVID-19 Vaccine (0.25 mL) booster dose in individuals who

completed primary vaccination with another authorized or approved COVID-19 Vaccine (heterologous booster dose) is inferred from the safety of a Moderna COVID-19 Vaccine (0.25 mL) booster dose administered following completion of a Moderna COVID-19 Vaccine primary series (homologous booster dose) and from data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose (0.5 mL) of the Moderna COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine (0.5 mL), Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Moderna COVID-19 Vaccine heterologous booster dose (0.5 mL) did not identify any new safety concerns, as compared with adverse reactions reported following Moderna COVID-19 Vaccine primary series doses or homologous booster dose (0.25 mL).

6.2 Post-Authorization Experience

The following adverse reactions have been identified during post-authorization use of the Moderna COVID-19 Vaccine. Because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Immune System Disorders: anaphylaxis
Nervous System Disorders: syncope

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for the MANDATORY reporting of the listed events following Moderna COVID-19 Vaccine to the Vaccine Adverse Event Reporting System (VAERS)

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome (MIS) in adults
- Cases of COVID-19 that results in hospitalization or death

*Serious Adverse Events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;

- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using one of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report, you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of Moderna COVID-19 Vaccine
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on Moderna COVID-19 Vaccine and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.
2. In Box 18, description of the event:
    a. Write “Moderna COVID-19 Vaccine EUA” as the first line
    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    b. In Box 14, provide the name and contact information of the best doctor/healthcare

professional to contact about the adverse event.

c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to ModernaTX, Inc. using the contact information below or by providing a copy of the VAERS form to ModernaTX, Inc.

Email	Fax number	Telephone number
ModernaPV@modernatx.com	1-866-599-1342	1-866-MODERNA (1-866-663-3762)

10 DRUG INTERACTIONS

There are no data to assess the concomitant administration of the Moderna COVID-19 Vaccine with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Moderna COVID-19 Vaccine during pregnancy. Women who are vaccinated with Moderna COVID-19 Vaccine during pregnancy are encouraged to enroll in the registry by calling 1-866-MODERNA (1-866-663-3762).

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (100 mcg) and other ingredients included in a single human dose of Moderna COVID-19 Vaccine was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. No vaccine-related adverse effects on female fertility, fetal development, or

postnatal development were reported in the study.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Safety and effectiveness have not been assessed in persons less than 18 years of age. Emergency Use Authorization of Moderna COVID-19 Vaccine does not include use in individuals younger than 18 years of age.

11.4 Geriatric Use

Clinical studies of Moderna COVID-19 Vaccine included participants 65 years of age and older receiving vaccine or placebo, and their data contribute to the overall assessment of safety and efficacy. In an ongoing Phase 3 clinical study (Study 1) of primary series dosing (0.5 mL), 24.8% (n=7,520) of participants were 65 years of age and older and 4.6% (n=1,399) of participants were 75 years of age and older. Vaccine efficacy in participants 65 years of age and older was 86.4% (95% CI 61.4, 95.2) compared to 95.6% (95% CI 90.6, 97.9) in participants 18 to <65 years of age *[see Clinical Trial Results and Supporting Data for EUA (18)]*. Overall, there were no notable differences in the safety profiles observed in participants 65 years of age and older and younger participants [see *Overall Safety Summary (6.1)]*.

In an ongoing Phase 2 clinical study (Study 2) of a single booster dose (0.25 mL), 22.2% (n=38) of participants were 65 years of age and older. This study did not include sufficient numbers of participants 65 years of age and older to determine whether they respond differently than younger participants. Some local and systemic adverse reactions were reported in a lower proportion of participants 65 years of age and older compared to participants 18 through 64 years of age *[see Overall Safety Summary (6.1)]*.

11.5 Use in Immunocompromised

In an independent study, safety and effectiveness of a third 0.5 mL primary series dose of the Moderna COVID-19 Vaccine have been evaluated in participants who received solid organ transplants *[see Overall Safety Summary (6.1) and Clinical Trial Results and Supporting Data for EUA (18.2)]*. The administration of a third primary series vaccine dose appears to be only moderately effective in increasing antibody titers. Patients should be counseled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated, as appropriate for their health status.

13 DESCRIPTION

Moderna COVID-19 Vaccine is provided as a white to off-white suspension for intramuscular injection.

Each 0.5 mL dose of Moderna COVID-19 Vaccine contains 100 mcg of nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus. Each 0.5 mL dose of the Moderna COVID-19 Vaccine contains the following ingredients: a total lipid content of 1.93 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.31 mg tromethamine, 1.18 mg tromethamine hydrochloride, 0.043 mg acetic acid, 0.20 mg sodium acetate trihydrate, and 43.5 mg sucrose. Each 0.25 mL dose of Moderna COVID-19 Vaccine contains half of these ingredients.

Moderna COVID-19 Vaccine does not contain a preservative.

The vial stoppers are not made with natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The nucleoside-modified mRNA in the Moderna COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Efficacy of Two-Dose Primary Series

Study 1 is an ongoing Phase 3 randomized, placebo-controlled, observer-blind clinical trial to evaluate the efficacy, safety, and immunogenicity of the Moderna COVID-19 Vaccine in participants 18 years of age and older in the United States (NCT04470427). Randomization was stratified by age and health risk: 18 to <65 years of age without comorbidities (not at risk for progression to severe COVID-19), 18 to <65 years of age with comorbidities (at risk for progression to severe COVID-19), and 65 years of age and older with or without comorbidities. Participants who were immunocompromised and those with a known history of SARS-CoV-2 infection were excluded from the study. Participants with no known history of SARS-CoV-2 infection but with positive laboratory results indicative of infection at study entry were included. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 30,420 participants were randomized equally to receive 2 doses of the Moderna COVID-19 Vaccine or saline placebo 1 month apart. Participants will be followed for efficacy and safety until 24 months after the second dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set) included 28,207 participants who received two doses (0.5 mL at 0 and 1 month) of either Moderna COVID-19 Vaccine (n=14,134) or placebo (n=14,073), and had a negative baseline SARS-CoV-2 status. In the Per-Protocol Set, 47.4% were female, 19.7% were Hispanic or Latino; 79.5% were White, 9.7% were African American, 4.6% were Asian, and 2.1% other races. The median age of participants was 53 years (range 18-95) and 25.3% of participants were 65 years of age and older. Of the study participants in the Per-Protocol Set, 18.5% were at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection) regardless of age. Between participants who received Moderna COVID-19 Vaccine and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

Efficacy Against COVID-19

COVID-19 was defined based on the following criteria: The participant must have experienced at least two of the following systemic symptoms: fever (≥38ºC / ≥100.4°F), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS- CoV-2 by RT-PCR. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

The median length of follow up for efficacy for participants in the study was 9 weeks post Dose 2. There were 11 COVID-19 cases in the Moderna COVID-19 Vaccine group and 185 cases in the placebo group, with a vaccine efficacy of 94.1% (95% confidence interval of 89.3% to 96.8%).

Table 5: Primary Efficacy Analysis: COVID-19* in Participants 18 Years of Age and Older Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)†
Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
14,134	11	3.328	14,073	185	56.510	94.1 (89.3, 96.8)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.
† VE and 95% CI from the stratified Cox proportional hazard model.

The subgroup analyses of vaccine efficacy are presented in Table 6.

Table 6: Subgroup Analyses of Vaccine Efficacy: COVID-19* Cases Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Age Subgroup (Years)	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)†
	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
18 to <65	10,551	7	2.875	10,521	156	64.625	95.6 (90.6, 97.9)
≥65	3,583	4	4.595	3,552	29	33.728	86.4 (61.4, 95.2)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.
† VE and 95% CI from the stratified Cox proportional hazard model.

Severe COVID-19 was defined based on confirmed COVID-19 as per the primary efficacy endpoint case definition, plus any of the following: Clinical signs indicative of severe systemic illness, respiratory rate ≥30 per minute, heart rate ≥125 beats per minute, SpO2 ≤93% on room air at sea level or PaO2/FIO2 <300 mm Hg; or respiratory failure or ARDS (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure <90 mmHg, diastolic BP <60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurologic dysfunction; or admission to an intensive care unit or death.

Among all participants in the Per-Protocol Set analysis, which included COVID-19 cases confirmed by an adjudication committee, no cases of severe COVID-19 were reported in the Moderna COVID-19 Vaccine group compared with 30 cases reported in the placebo group (incidence rate 9.138 per 1,000 person-years). One PCR-positive case of severe COVID-19 in a vaccine recipient was awaiting adjudication at the time of the analysis.

18.2 Immunogenicity in Solid Organ Transplant Recipients

An independent randomized-controlled study has been conducted in 120 participants who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years previously (range 1.99-6.75 years). A third 0.5 mL primary series dose of the Moderna COVID-19 Vaccine was administered to 60 participants approximately 2 months after they had received a second dose; saline placebo was given to 60 individuals for comparison. Significant increases in levels of SARS-CoV-2 antibodies occurred four weeks after the third dose in 55.0% of participants in the Moderna COVID-19 Vaccine group (33 of 60) and 17.5% of participants in the placebo group (10 of 57).

18.3 Immunogenicity of a Booster Dose Following a Moderna COVID-19 Vaccine Primary Series

Effectiveness of a booster dose of the Moderna COVID-19 Vaccine was based on assessment of neutralizing antibody titers (ID50) against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation. Immunogenicity analyses compared the ID50 following the booster dose to the ID50 following the primary series.

In an open-label phase of Study 2, participants 18 years of age and older received a single booster dose (0.25 mL) at least 6 months after completion of the primary series (two doses of 0.5 mL 1 month apart). The primary immunogenicity analysis population included 149 booster dose participants in Study 2 (including one individual who had only received a single dose of the primary series) and a random subset of 1055 participants from Study 1 who received two doses (0.5 mL 1 month apart) of Moderna COVID-19 Vaccine. Study 1 and 2 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. Among participants assessed for immunogenicity, 60.4% were female, 6.7% were Hispanic or Latino; 95.3% were White, 3.4% were Black or African American, 0.7% were Asian, and 0.7% were American Indian or Alaskan Native; 9.4% were obese (body mass index ≥30 kg/m^2). The median age of Study 2 participants was 56 years of age (range 18-82) and 24.8% of participants were 65 years of age and older. Study 2 participants included in the primary immunogenicity analysis population did not have pre-existing medical conditions that would place them at risk of severe COVID-19. Study 1 participants included in the primary immunogenicity analysis population were a stratified random sample which reflected the overall primary efficacy analysis population with regards to demographics and pre-existing medical conditions with a higher percentage of those ≥65 years of age (33.6%), with risk factors for severe COVID-19 (39.4%), and communities of color (53.5%).

Immunogenicity analyses included an assessment of ID50 geometric mean titer (GMT) ratio and difference in seroresponse rates. The analysis of the GMT ratio of ID50 following the booster dose compared to the primary series met the immunobridging criteria for a booster response. Seroresponse for a participant was defined as achieving a ≥4-fold rise in ID50 from baseline (before the booster dose in Study 2 and before the first dose of the primary series in Study 1). The lower limit of the 2-sided 95% CI for the difference in seroresponse rates between Study 1 and Study 2 was -16.7%, which did not meet the immunobridging criterion for a booster response (lower limit of 2-sided 95% CI for the percentage difference of ≥ -10%). These analyses are summarized in Tables 7 and 8.

Table 7: Neutralizing Antibody Geometric Mean Titers (ID50) Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days After a Booster Dose in Study 2 vs 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Dose N[a]=149 GMT[b] (95% CI)	**Study 1 Primary Series N[a]=1053 GMT[b] (95% CI)**	**GMT Ratio (Study 2/Study 1)**	**Met Success Criteria[c]**
1802 (1548, 2099)	1027 (968, 1089)	1.8 (1.5, 2.1)	Lower limit of 95% CI ≥0.67 Criterion: Yes Point Estimate ≥1.0 Criterion: Yes

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study 2 Day 1 for Study 2) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study 2 Day 1 for Study 2), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study 2 and Day 57 for Study 1).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Given the lack of randomization in Study 2, the statistical analysis plan pre-specified an analysis of covariance model for estimating the geometric mean titer that adjusts for differences in age groups (<65 years, ≥65 years).

[c] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the GMR is >0.67 and the point estimate of the GLSM ratio is ≥1.0.

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

GLSM = Geometric least squares mean

GMR = Geometric mean ratio

Table 8: Seroresponse Rates Against A Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days Post-Booster Dose in Study 2 and 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Seroresponse[a] N[b]=149 n (%) (95% CI)[c]	**Study 1 Primary Series Seroresponse[a] N[b]=1050 n (%) (95% CI)[c]**	**Difference in Seroresponse Rate (Study 2-Study 1) % (95% CI)[d]**	**Met Success Criterion[e]**
131 (87.9) (81.6, 92.7)	1033 (98.4) (97.4, 99.1)	-10.5 (-16.7, -6.1)	Lower limit of 95% CI ≥-10% Criterion: No

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study 2 Day 1 for Study 2) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study 2 Day 1 for Study 2), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study 2 and Day 57 for Study 1).

[a] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody titers (ID50) from baseline (pre-booster dose in Study 2 and pre-dose 1 in Study 1), where baseline titers < LLOQ are set to LLOQ for the analysis.

[b] Number of subjects with non-missing data at both baseline and the post-baseline timepoint of interest.

[c] 95% CI is calculated using the Clopper-Pearson method.

[d] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[e] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the percentage difference is > -10%.

Study 2 participants who met the ≥4-fold increase in titer post-booster dose (87.9%) had a lower baseline GMT of 109 (range of individual titers 9, 4393), whereas Study 2 participants who did not meet the ≥4-fold increase in titers post-booster had a higher baseline GMT of 492 (range of individual titers 162, 2239).

An additional descriptive analysis evaluated seroresponse rates using baseline neutralizing antibody titers prior to dose 1 of the primary series. As shown in Table 9 below, the booster dose seroresponse rate, with seroresponse defined as at least a 4-fold rise relative to the pre-dose 1 titer, was 100%. The difference in seroresponse rates in this post-hoc analysis was 1.6% (95% CI -0.9, 2.6).

Table 9: Analysis of Seroresponse Rates Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days Post-Booster Dose in Study 2 and 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Seroresponse[a] N[b]=148 n (%) (95% CI)[d]	**Study 1 Primary Series Seroresponse[a] N[c]=1050 n (%) (95% CI)[d]**	**Difference in Seroresponse Rate (After Booster-After Primary Series) % (95% CI)[e]**
148 (100) (97.5, 100)	1033 (98.4) (97.4, 99.1)	1.6 (-0.9, 2.6)

* Per-Protocol Immunogenicity Set included all subjects who had non-missing data at baseline (before dose 1) and 28 days post-booster in Study 2 or 28 days post-dose 2 in the primary series in Study 1, respectively, did not have SARS-CoV-2 infection at pre-booster in Study 2 or baseline in Study 1, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest.

[a] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody titers (ID50) from pre-dose 1, where baseline titers < LLOQ are set to LLOQ for the analysis.

[b] Number of subjects with non-missing data at baseline (before dose 1) and 28 days post-booster in Study 2.

[c] Number of subjects with non-missing data at baseline (before dose 1) and 28 days post-dose 2 in the primary series in Study 1.

[d] 95% CI is calculated using the Clopper-Pearson method.

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

18.4 Immunogenicity of a Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

Effectiveness of a Moderna COVID-19 Vaccine (0.25 mL) booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 Vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Moderna COVID-19 Vaccine (0.25 mL) booster dose administered following completion of a Moderna COVID-19 Vaccine primary series and from immunogenicity data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose (0.5 mL) of the Moderna COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to

enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Moderna COVID-19 Vaccine (0.5 mL) was demonstrated regardless of primary vaccination.

19 HOW SUPPLIED/STORAGE AND HANDLING

Moderna COVID-19 Vaccine Suspension for Intramuscular Injection Multiple-Dose Vials are supplied as follows:

NDC 80777-273-99 Carton of 10 multiple-dose vials, each vial containing 5.5 mL

NDC 80777-273-98 Carton of 10 multiple-dose vials, each vial containing 7.5 mL

During storage, minimize exposure to room light.

Store frozen between -50º to -15ºC (-58º to 5ºF). Store in the original carton to protect from light.

Do not store on dry ice or below -50ºC (-58ºF). Use of dry ice may subject vials to temperatures colder than -50°C (-58°F).

Vials may be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use. Do not refreeze.

Vials may be stored between 8° to 25°C (46° to 77°F) for a total of 24 hours.

After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Vials should be discarded 12 hours after the first puncture.

Thawed vials can be handled in room light conditions.

Do not refreeze once thawed.

Transportation of Thawed Vials at 2° to 8°C (36° to 46°F)

If transport at -50° to -15°C (-58° to 5°F) is not feasible, available data support transportation of one or more thawed vials for up to 12 hours at 2° to 8°C (36° to 46°F) when shipped using shipping containers which have been qualified to maintain 2° to 8°C (36° to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. Once thawed and transported at 2° to 8°C (36° to 46°F), vials should not be refrozen and should be stored at 2° to 8°C (36° to 46°F) until use.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at: https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions, send an email or call the telephone number provided below.

Email	Telephone number
medinfo@modernatx.com	1-866-MODERNA (1-866-663-3762)

This EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please visit www.modernatx.com/covid19vaccine-eua.

Moderna US, Inc.
Cambridge, MA 02139

Patent(s): www.modernatx.com/patents
Revised: Oct/20/2021

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

FOR 12 YEARS OF AGE AND OLDER
DILUTE BEFORE USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 5 years of age and older.

There are 2 formulations of Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 12 years of age of older:

> **The formulation supplied in a multiple dose vial with a purple cap MUST BE DILUTED PRIOR TO USE.**
>
> **The formulation supplied in a multiple dose vial with a gray cap and label with a gray border IS NOT DILUTED PRIOR TO USE.**

This Fact Sheet pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap, which is authorized for use in individuals 12 years of age and older, and MUST BE DILUTED PRIOR TO USE.

Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap is authorized for use to provide:

- **a 2-dose primary series to individuals 12 years of age and older;**
- **a third primary series dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise; and**
- **a single booster dose to the following individuals who have completed a primary series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY:**
    - **65 years of age and older**
    - **18 through 64 years of age at high risk of severe COVID-19**
    - **18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2**
- **a single booster dose to eligible individuals who have completed primary vaccination with a different authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.**

COMIRNATY (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine made by Pfizer for BioNTech that is indicated for active immunization to prevent COVID-19 in individuals 16 years of age and older. It is approved for use as a 2-dose primary series for the prevention of COVID-19 in individuals 16 years of age and older. It is also authorized for emergency use to provide:

- **a 2-dose primary series to individuals 12 through 15 years;**
- **a third primary series dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise; and**
- **a single booster dose to the following individuals who have completed a primary series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY:**
    - **65 years of age and older**
    - **18 through 64 years of age at high risk of severe COVID-19**
    - **18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2**
- **a single booster dose to eligible individuals who have completed primary vaccination with a different authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.**

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine for ages 12 years and older when prepared according to their respective instructions for use can be used interchangeably.[1]

COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine intended for individuals ages 12 years and older should not be used for individuals 5 through 11 years of age because of the potential for vaccine administration errors, including dosing errors.[2]

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

[1] When prepared according to their respective instructions for use, the FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine for ages 12 years of age and older can be used interchangeably without presenting any safety or effectiveness concerns.

[2] Notwithstanding the age limitations for use of the different formulations and presentations described above, individuals who will turn from 11 years to 12 years of age between their first and second dose in the primary regimen may receive, for either dose, either: (1) the Pfizer-BioNTech COVID-19 Vaccine formulation authorized for use in individuals 5 through 11 years of age (each 0.2 mL dose containing 10 mcg modRNA) (orange cap); or (2) COMIRNATY or one of the Pfizer-BioNTech COVID-19 Vaccine formulations authorized for use in individuals 12 years of age and older (each 0.3 mL dose containing 30 mcg modRNA) (gray and purple cap).

Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine. See "MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

The Pfizer-BioNTech COVID-19 Vaccine is a suspension for intramuscular injection.

Primary Series

The Pfizer-BioNTech COVID-19 Vaccine is administered as a primary series of 2 doses (0.3 mL each) 3 weeks apart in individuals 12 years of age or older.

A third primary series dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) at least 28 days following the second dose is authorized for administration to individuals at least 12 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose

A single Pfizer-BioNTech COVID-19 Vaccine booster dose (0.3 mL) may be administered intramuscularly at least 6 months after completing the primary series to individuals:

- 65 years of age and older
- 18 through 64 years of age at high risk of severe COVID-19
- 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2

A single booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be administered as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.cvdvaccine.com.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine for active immunization against COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

The storage, preparation, and administration information in this Fact Sheet apply to the Pfizer-BioNTech COVID-19 Vaccine for 12 years of age and older, which is supplied in a multiple dose vial with a purple cap and **MUST BE DILUTED** before use.

Pfizer-BioNTech COVID-19 Vaccine, Multiple Dose Vial with Purple Cap

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
12 years and older	Dilute with 1.8 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	6	0.3 mL

Storage and Handling

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with purple caps arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. This information in the package insert supersedes the storage conditions printed on the vial cartons.

Cartons and vials of Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps with an expiry date of July 2021 through February 2022 printed on the label may remain in use for 3 months beyond the printed date as long as approved storage conditions between -90ºC to -60ºC (-130ºF to -76ºF) have been maintained. Updated expiry dates are shown below.

Printed Expiry Date		Updated Expiry Date
July 2021	→	October 2021
August 2021	→	November 2021
September 2021	→	December 2021
October 2021	→	January 2022
November 2021	→	February 2022
December 2021	→	March 2022
January 2022	→	April 2022
February 2022	→	May 2022

If not stored between -90ºC to -60ºC (-130ºF to -76ºF), vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration
Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature
For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions. Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

- After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution.
- During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.
- Any vaccine remaining in vials must be discarded after 6 hours.
- Do not refreeze.

Dosing and Schedule

Primary Series

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a primary series of 2 doses (0.3 mL each) 3 weeks apart to individuals 12 years of age and older.

A third primary series dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) at least 28 days following the second dose is authorized for administration to individuals at least 12 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose

A single Pfizer-BioNTech COVID-19 Vaccine booster dose (0.3 mL) may be administered intramuscularly at least 6 months after completing the primary series to individuals:

- 65 years of age and older
- 18 through 64 years of age at high risk of severe COVID-19
- 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2

A single booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be administered as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine for ages 12 years and older when prepared according to their respective instructions for use, can be used interchangeably.

COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine intended for individuals ages 12 years and older should not be used for individuals 5 through 11 years of age because of the potential for vaccine administration errors, including dosing errors.

<u>Dose Preparation</u>

Each vial **MUST BE DILUTED** before administering the vaccine.

Prior to Dilution

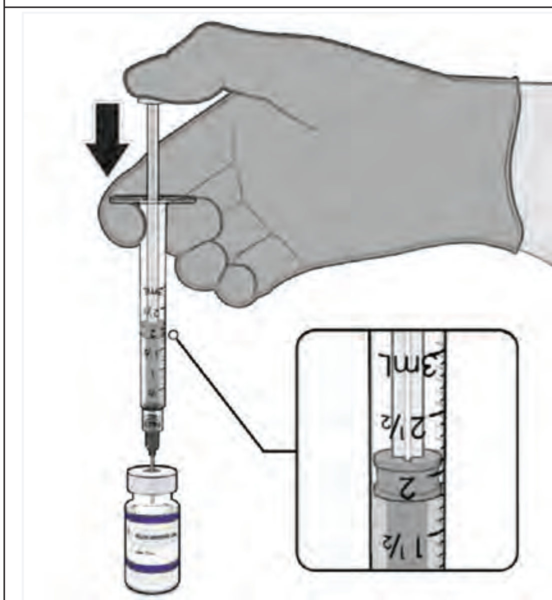
- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial with a purple cap contains a volume of 0.45 mL and is supplied as a frozen suspension that does not contain preservative.
- Each vial must be thawed before dilution.
    - Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *(see Storage and Handling)*.
    - Refer to thawing instructions in the panels below.

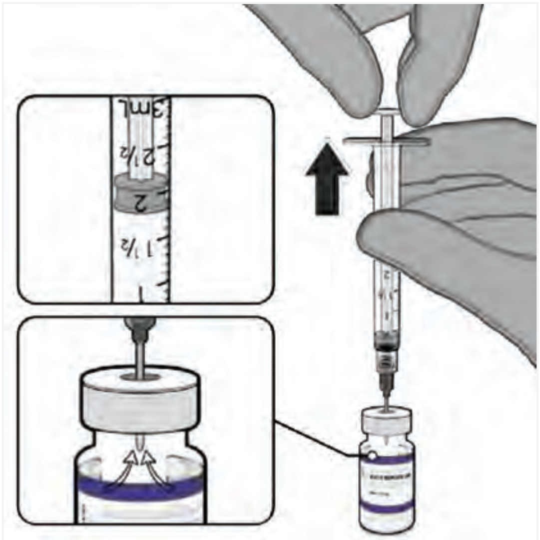
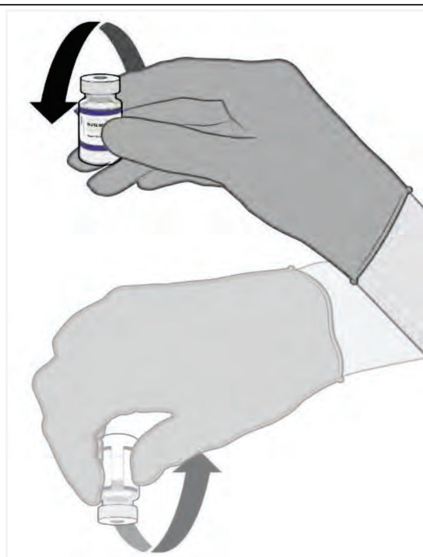
Dilution

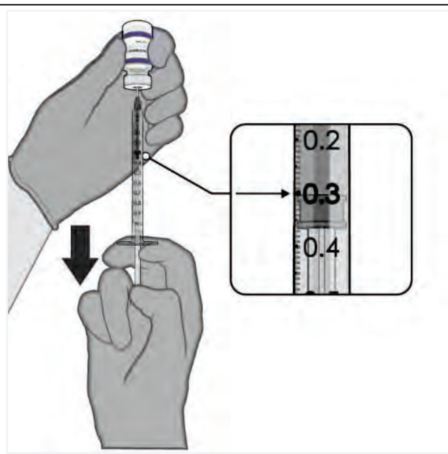
Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. <u>Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent</u>. Do not add more than 1.8 mL of diluent.

After dilution, 1 vial contains 6 doses of 0.3 mL.

<table>
<tr><th colspan="2">Dilution and Preparation Instructions</th></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap –
VIAL VERIFICATION</td></tr>
<tr><td>
✓ Purple plastic cap and purple label border.</td><td>Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine has a purple plastic cap. Some vials also may have a purple label border.</td></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap –
THAWING PRIOR TO DILUTION</td></tr>
<tr><td>
</td><td>• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
  ○ Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month.
  ○ Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.</td></tr>
</table>

Dilution and Preparation Instructions	
 **Gently × 10**	• Before dilution invert vaccine vial gently 10 times. • <u>Do not shake</u>. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – DILUTION	
 **Add 1.8 mL of sterile 0.9% sodium chloride injection, USP.**	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.

Dilution and Preparation Instructions	
 **Pull back plunger to 1.8 mL to remove air from vial.**	Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.
 **Gently × 10**	• Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.

Dilution and Preparation Instructions	
 **Record the date and time of dilution.** **Use within 6 hours after dilution.**	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – WITHDRAWAL OF INDIVIDUAL 0.3 mL DOSES	
 **Withdraw 0.3 mL dose of vaccine.**	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw <u>0.3 mL</u> of the Pfizer-BioNTech COVID-19 Vaccine preferentially using a low dead-volume syringe and/or needle. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

Administration

Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine with purple caps contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 6 doses from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and content.
- Do not pool excess vaccine from multiple vials.

Contraindications

Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine *(see Full EUA Prescribing Information)*.

Warnings

Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine.

Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.

Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine.

Limitation of Effectiveness

Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

Adverse Reactions

Adverse Reactions in Clinical Trials
Adverse reactions following administration of the Pfizer-BioNTech COVID-19 Vaccine that have been reported in clinical trials include injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling, injection site redness, nausea, malaise, lymphadenopathy, decreased appetite, rash, and pain in extremity *(see Full EUA Prescribing Information)*.

Adverse Reactions in Post Authorization Experience
Severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema), diarrhea, vomiting, pain in extremity (arm), and syncope have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Pfizer-BioNTech COVID-19 Vaccine.

Use with Other Vaccines

There is no information on the co-administration of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Vaccine Information Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.cvdvaccine.com to obtain the Vaccine Information Fact Sheet) prior to the individual receiving each dose of the Pfizer-BioNTech COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine, which is not an FDA-approved vaccine.
- The recipient or their caregiver has the option to accept or refuse Pfizer-BioNTech COVID-19 Vaccine.
- The significant known and potential risks and benefits of the Pfizer-BioNTech COVID-19 Vaccine, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of Pfizer-BioNTech COVID-19 Vaccine.

Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION[3]

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of Pfizer-BioNTech COVID-19 Vaccine, the following items are required. Use of unapproved Pfizer-BioNTech COVID-19 Vaccine for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. Pfizer-BioNTech COVID-19 Vaccine is authorized for use in individuals 5 years of age and older.

[3] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

2. The vaccination provider must communicate to the individual receiving the Pfizer-BioNTech COVID-19 Vaccine or their caregiver, information consistent with the "Vaccine Information Fact Sheet for Recipients and Caregivers" prior to the individual receiving Pfizer-BioNTech COVID-19 Vaccine.

3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):
   - vaccine administration errors whether or not associated with an adverse event,
   - serious adverse events* (irrespective of attribution to vaccination),
   - cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and
   - cases of COVID-19 that result in hospitalization or death.

   Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. The reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of MIS in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine to recipients.

* Serious adverse events are defined as:
- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent 1 of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND PFIZER INC.

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

ADDITIONAL INFORMATION

For general questions, visit the website or call the telephone number provided below.

To access the most recent Pfizer-BioNTech COVID-19 Vaccine Fact Sheets, please scan the QR code provided below.

Global website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

AVAILABLE ALTERNATIVES

COMIRNATY (COVID-19 Vaccine, mRNA) is an FDA-approved vaccine to prevent COVID-19 caused by SARS-CoV-2. There may be clinical trials or availability under EUA of other COVID-19 vaccines.

COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine intended for individuals ages 12 years and older should not be used for individuals 5 through 11 years of age because of the potential for vaccine administration errors, including dosing errors.

FEDERAL COVID-19 VACCINATION PROGRAM

This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for

administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, Health Resources & Services Administration [HRSA] COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or https://TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. In response, FDA has issued an EUA for the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, and for certain uses of FDA-approved COMIRNATY for active immunization against COVID-19.

FDA issued this EUA, based on Pfizer-BioNTech's request and submitted data.

For the authorized uses, although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

The Countermeasures Injury Compensation Program

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the Pfizer-BioNTech COVID-19 Vaccine used to prevent COVID-19, visit www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Manufactured by
Pfizer Inc., New York, NY 10017

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

LAB-1450-15.2

Revised: 29 October 2021

END SHORT VERSION FACT SHEET
Long Version (Full EUA Prescribing Information) Begins On Next Page

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

PFIZER-BIONTECH COVID-19 VACCINE

FULL EMERGENCY USE AUTHORIZATION PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full emergency use authorization prescribing information are not listed.

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

Pfizer-BioNTech COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 5 years of age and older.

This Fact Sheet pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap, which is authorized for use in individuals 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

The storage, preparation, and administration information in this Prescribing Information apply to the Pfizer-BioNTech COVID-19 Vaccine for 12 years of age and older, which is supplied in a multiple dose vial with a purple cap and **MUST BE DILUTED** before use.

Pfizer-BioNTech COVID-19 Vaccine, Multiple Dose Vial with Purple Cap

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
12 years and older	Dilute with 1.8 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	6	0.3 mL

2.1 Preparation for Administration

Dose Preparation

Each vial **MUST BE DILUTED** before administering the vaccine.

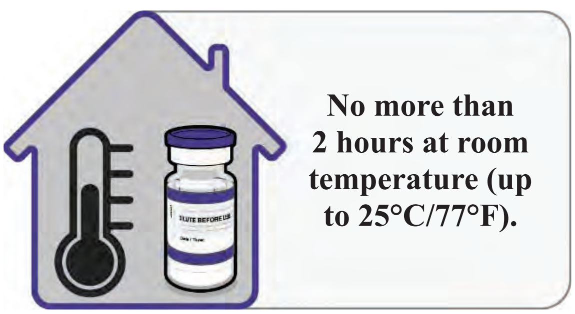
Prior to Dilution

- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial with a purple cap contains a volume of 0.45 mL and is supplied as a frozen suspension that does not contain preservative.
- Each vial must be thawed before dilution.
    - Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see o Supplied Storage and andling (1)]*.
    - Refer to thawing instructions in the panels below.

Dilution

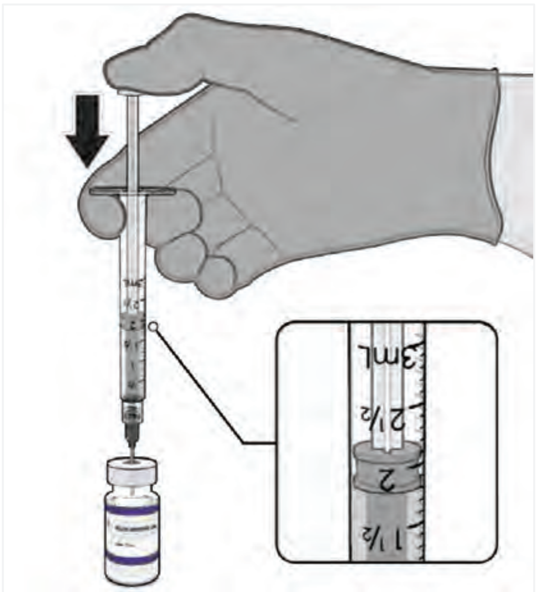
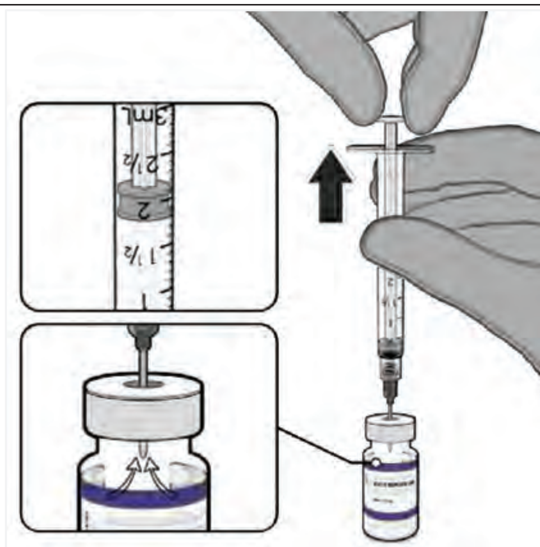
- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride

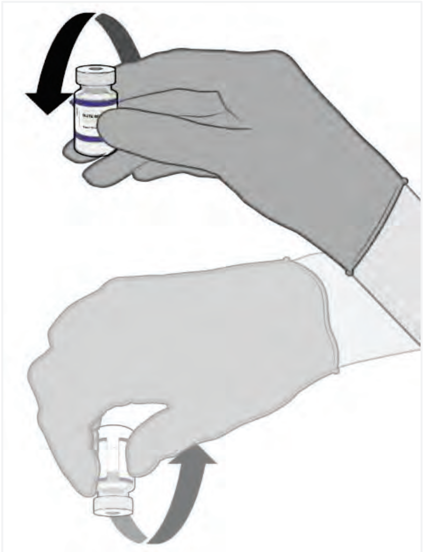
Injection or any other diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.

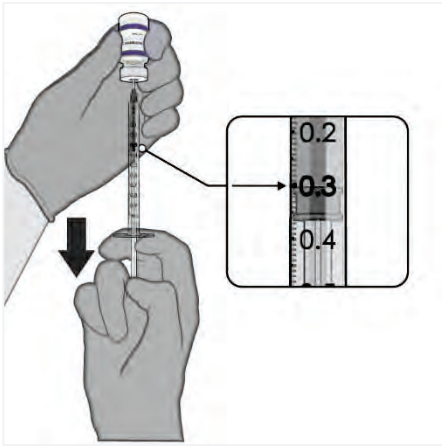
<table>
<tr><td colspan="2">Dilution and Preparation Instructions</td></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap –
VIAL VERIFICATION</td></tr>
<tr><td>
✓ Purple plastic cap and purple label border.</td><td>Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine has a purple plastic cap. Some vials also may have a purple label border on the label.</td></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap –
THAWING PRIOR TO DILUTION</td></tr>
<tr><td>
</td><td>• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month.
o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.</td></tr>
<tr><td>
Gently × 10</td><td>• Before dilution invert vaccine vial gently 10 times.
• <u>Do not shake</u>.
• Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
• Do not use if liquid is discolored or if other particles are observed.</td></tr>
</table>

Dilution and Preparation Instructions

Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – DILUTION

 **Add 1.8 mL of sterile 0.9% sodium chloride injection, USP.**	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
 **Pull back plunger to 1.8 mL to remove air from vial.**	Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

Dilution and Preparation Instructions	
 **Gently × 10**	• Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
 **Record the date and time of dilution.** **Use within 6 hours after dilution.**	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

Dilution and Preparation Instructions	
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – WITHDRAWAL OF INDIVIDUAL 0.3 mL DOSES	
 **Withdraw 0.3 mL dose of vaccine.**	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer-BioNTech COVID-19 Vaccine preferentially using a low dead-volume syringe and/or needle. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine with purple caps contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 6 doses from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

Primary Series

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a primary series of 2 doses (0.3 mL each) 3 weeks apart in individuals 12 years of age and older.

A third primary series dose of the Pfizer-BioNTech COVID-19 vaccine (0.3 mL) at least 28 days following the second dose is authorized for administration to individuals at least 12 years of age who have undergone solid

organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose

A single Pfizer-BioNTech COVID-19 Vaccine booster dose (0.3 mL) may be administered intramuscularly at least 6 months after completing the primary series to individuals:

- 65 years of age and older
- 18 through 64 years of age at high risk of severe COVID-19
- 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2

A single booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be administered as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine for ages 12 years of age and older when prepared according to their respective instructions for use, can be used interchangeably.

COMIRNATY (COVID-19 Vaccine, mRNA) and the two EUA-authorized formulations of Pfizer-BioNTech COVID-19 Vaccine intended for individuals ages 12 years and older should not be used for individuals 5 through 11 years of age because of the potential for vaccine administration errors, including dosing errors.

3 DOSAGE FORMS AND STRENGTHS

Pfizer-BioNTech COVID-19 Vaccine is a suspension for injection.

After preparation, each dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in vials with purple caps is 0.3 mL for individuals 12 years of age and older *[see Dosage and Administration (2.1)]*.

4 CONTRAINDICATIONS

Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine.

Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine.

5.5 Limitation of Effectiveness

The Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and hospitalized or fatal cases of COVID-19 following vaccination with the Pfizer-BioNTech COVID-19 Vaccine.[4] To the extent feasible, provide a copy of the VAERS form to Pfizer Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and Pfizer Inc.

Primary Series

In clinical studies of participants 16 years of age and older who received Pfizer-BioNTech COVID-19 Vaccine containing 30 mcg of a nucleoside-modified messenger RNA encoding the viral spike (S) glycoprotein of SARS-CoV-2 (30 mcg modRNA), adverse reactions following administration of the primary series included pain at the injection site (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%), injection site swelling (10.5%), injection site redness (9.5%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%).

In a clinical study in adolescents 12 through 15 years of age who received Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA), adverse reactions following administration of the primary series included pain at the injection site (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%),

[4] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

joint pain (20.2%), injection site swelling (9.2%), injection site redness (8.6%), lymphadenopathy (0.8%), and nausea (0.4%).

Booster Dose

In a clinical study of participants 18 through 55 years of age, adverse reactions following administration of a booster dose were pain at the injection site (83.0%), fatigue (63.7%), headache (48.4%), muscle pain (39.1%), chills (29.1%), joint pain (25.3%), lymphadenopathy (5.2%), nausea (0.7%), decreased appetite (0.3%), rash (0.3%), and pain in extremity (0.3%).

Post Authorization Experience

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Primary Series

The safety of the primary series Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 12 years of age and older in two clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America.

Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age. Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 43,448 participants [21,720 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2; 21,728 placebo] in Phase 2/3 are 16 years of age or older (including 138 and 145 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively) and 2,260 adolescents are 12 through 15 years of age (1,131 and 1,129 in the vaccine and placebo groups, respectively).

In Study 2, all participants 12 to <16 years of age, and 16 years of age and older in the reactogenicity subset, were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination]. Tables 1 through 6 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of Pfizer-BioNTech COVID 19 Vaccine and placebo.

Participants 16 ears of Age and Older

At the time of the analysis of Study 2 for the EUA, 37,586 (18,801 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) and 18,785 placebo) participants 16 years of age or older had been followed for a median of 2 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants 16 years and older enrolled by October 9, 2020, and includes safety data accrued through November 14, 2020.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the total participants who received either the Pfizer-BioNTech COVID-19 Vaccine or placebo, 50.6% were male and 49.4% were female, 83.1% were White, 9.1% were Black or African American, 28.0% were Hispanic/Latino, 4.3% were Asian, and 0.5% were American Indian/Alaska Native.

Solicited ocal and Systemic Adverse Reactions

Across both age groups, 18 through 55 years of age and 56 years and older, the mean duration of pain at the injection site after Dose 2 was 2.5 days (range 1 to 36 days), for redness 2.6 days (range 1 to 34 days), and for swelling 2.3 days (range 1 to 34 days) for participants in the Pfizer-BioNTech COVID-19 Vaccine group.

Solicited reactogenicity data in 16 and 17 year-old participants are limited.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 18 Through 55 Years of Age‡ – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=2291 n[b] (%)	**Placebo Dose 1 N[a]=2298 n[b] (%)**	**Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=2098 n[b] (%)**	**Placebo Dose 2 N[a]=2103 n[b] (%)**
Redness[c]				
Any (>2 cm)	104 (4.5)	26 (1.1)	123 (5.9)	14 (0.7)
Mild	70 (3.1)	16 (0.7)	73 (3.5)	8 (0.4)
Moderate	28 (1.2)	6 (0.3)	40 (1.9)	6 (0.3)
Severe	6 (0.3)	4 (0.2)	10 (0.5)	0 (0.0)
Swelling[c]				
Any (>2 cm)	132 (5.8)	11 (0.5)	132 (6.3)	5 (0.2)
Mild	88 (3.8)	3 (0.1)	80 (3.8)	3 (0.1)
Moderate	39 (1.7)	5 (0.2)	45 (2.1)	2 (0.1)
Severe	5 (0.2)	3 (0.1)	7 (0.3)	0 (0.0)

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Pain at the injection site[d]				
Any	1904 (83.1)	322 (14.0)	1632 (77.8)	245 (11.7)
Mild	1170 (51.1)	308 (13.4)	1039 (49.5)	225 (10.7)
Moderate	710 (31.0)	12 (0.5)	568 (27.1)	20 (1.0)
Severe	24 (1.0)	2 (0.1)	25 (1.2)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
‡ Eight participants were between 16 and 17 years of age.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 18 Through 55 Years of Age‡ – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Fever				
≥38.0°C	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
≥38.0°C to 38.4°C	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4°C to 38.9°C	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9°C to 40.0°C	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0°C	0 (0.0)	2 (0.1)	1 (0.0)	0 (0.0)
Fatigue[c]				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)
Mild	597 (26.1)	467 (20.3)	442 (21.1)	248 (11.8)
Moderate	455 (19.9)	289 (12.6)	708 (33.7)	217 (10.3)
Severe	33 (1.4)	11 (0.5)	97 (4.6)	14 (0.7)
Headache[c]				
Any	959 (41.9)	775 (33.7)	1085 (51.7)	506 (24.1)
Mild	628 (27.4)	505 (22.0)	538 (25.6)	321 (15.3)
Moderate	308 (13.4)	251 (10.9)	480 (22.9)	170 (8.1)
Severe	23 (1.0)	19 (0.8)	67 (3.2)	15 (0.7)
Chills[c]				
Any	321 (14.0)	146 (6.4)	737 (35.1)	79 (3.8)
Mild	230 (10.0)	111 (4.8)	359 (17.1)	65 (3.1)
Moderate	82 (3.6)	33 (1.4)	333 (15.9)	14 (0.7)
Severe	9 (0.4)	2 (0.1)	45 (2.1)	0 (0.0)

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Vomiting[d]				
Any	28 (1.2)	28 (1.2)	40 (1.9)	25 (1.2)
Mild	24 (1.0)	22 (1.0)	28 (1.3)	16 (0.8)
Moderate	4 (0.2)	5 (0.2)	8 (0.4)	9 (0.4)
Severe	0 (0.0)	1 (0.0)	4 (0.2)	0 (0.0)
Diarrhea[e]				
Any	255 (11.1)	270 (11.7)	219 (10.4)	177 (8.4)
Mild	206 (9.0)	217 (9.4)	179 (8.5)	144 (6.8)
Moderate	46 (2.0)	52 (2.3)	36 (1.7)	32 (1.5)
Severe	3 (0.1)	1 (0.0)	4 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	487 (21.3)	249 (10.8)	783 (37.3)	173 (8.2)
Mild	256 (11.2)	175 (7.6)	326 (15.5)	111 (5.3)
Moderate	218 (9.5)	72 (3.1)	410 (19.5)	59 (2.8)
Severe	13 (0.6)	2 (0.1)	47 (2.2)	3 (0.1)
New or worsened joint pain[c]				
Any	251 (11.0)	138 (6.0)	459 (21.9)	109 (5.2)
Mild	147 (6.4)	95 (4.1)	205 (9.8)	54 (2.6)
Moderate	99 (4.3)	43 (1.9)	234 (11.2)	51 (2.4)
Severe	5 (0.2)	0 (0.0)	20 (1.0)	4 (0.2)
Use of antipyretic or pain medication[f]	638 (27.8)	332 (14.4)	945 (45.0)	266 (12.6)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.
‡ Eight participants were between 16 and 17 years of age.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Redness[c]				
Any (>2 cm)	85 (4.7)	19 (1.1)	120 (7.2)	12 (0.7)
Mild	55 (3.1)	12 (0.7)	59 (3.6)	8 (0.5)
Moderate	27 (1.5)	5 (0.3)	53 (3.2)	3 (0.2)
Severe	3 (0.2)	2 (0.1)	8 (0.5)	1 (0.1)
Swelling[c]				
Any (>2 cm)	118 (6.5)	21 (1.2)	124 (7.5)	11 (0.7)
Mild	71 (3.9)	10 (0.6)	68 (4.1)	5 (0.3)
Moderate	45 (2.5)	11 (0.6)	53 (3.2)	5 (0.3)
Severe	2 (0.1)	0 (0.0)	3 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2 cm)	1282 (71.1)	166 (9.3)	1098 (66.1)	127 (7.7)
Mild	1008 (55.9)	160 (8.9)	792 (47.7)	125 (7.6)
Moderate	270 (15.0)	6 (0.3)	298 (18.0)	2 (0.1)
Severe	4 (0.2)	0 (0.0)	8 (0.5)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Fever				
≥38.0℃	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
≥38.0℃ to 38.4℃	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4℃ to 38.9℃	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9℃ to 40.0℃	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0℃	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[c]				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)
Mild	373 (20.7)	252 (14.1)	351 (21.1)	161 (9.8)
Moderate	240 (13.3)	150 (8.4)	442 (26.6)	114 (6.9)
Severe	2 (0.1)	3 (0.2)	46 (2.8)	2 (0.1)

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Headache[c]				
Any	454 (25.2)	325 (18.1)	647 (39.0)	229 (13.9)
Mild	348 (19.3)	242 (13.5)	422 (25.4)	165 (10.0)
Moderate	104 (5.8)	80 (4.5)	216 (13.0)	60 (3.6)
Severe	2 (0.1)	3 (0.2)	9 (0.5)	4 (0.2)
Chills[c]				
Any	113 (6.3)	57 (3.2)	377 (22.7)	46 (2.8)
Mild	87 (4.8)	40 (2.2)	199 (12.0)	35 (2.1)
Moderate	26 (1.4)	16 (0.9)	161 (9.7)	11 (0.7)
Severe	0 (0.0)	1 (0.1)	17 (1.0)	0 (0.0)
Vomiting[d]				
Any	9 (0.5)	9 (0.5)	11 (0.7)	5 (0.3)
Mild	8 (0.4)	9 (0.5)	9 (0.5)	5 (0.3)
Moderate	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Diarrhea[e]				
Any	147 (8.2)	118 (6.6)	137 (8.3)	99 (6.0)
Mild	118 (6.5)	100 (5.6)	114 (6.9)	73 (4.4)
Moderate	26 (1.4)	17 (0.9)	21 (1.3)	22 (1.3)
Severe	3 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	251 (13.9)	149 (8.3)	477 (28.7)	87 (5.3)
Mild	168 (9.3)	100 (5.6)	202 (12.2)	57 (3.5)
Moderate	82 (4.6)	46 (2.6)	259 (15.6)	29 (1.8)
Severe	1 (0.1)	3 (0.2)	16 (1.0)	1 (0.1)
New or worsened joint pain[c]				
Any	155 (8.6)	109 (6.1)	313 (18.9)	61 (3.7)
Mild	101 (5.6)	68 (3.8)	161 (9.7)	35 (2.1)
Moderate	52 (2.9)	40 (2.2)	145 (8.7)	25 (1.5)
Severe	2 (0.1)	1 (0.1)	7 (0.4)	1 (0.1)
Use of antipyretic or pain medication	358 (19.9)	213 (11.9)	625 (37.7)	161 (9.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.
a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

From an independent report (*amar Abravanel F arion O et al. Three doses of an mR A Covid-1 vaccine in solid-organ transplant recipients. Engl ed)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third

vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Serious Adverse Events
In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (Pfizer-BioNTech COVID-19 Vaccine = 10,841; placebo = 10,851), serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.3% of placebo recipients. In a similar analysis, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 7,960, placebo = 7,934), serious adverse events were reported by 0.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.6% of placebo recipients who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

Appendicitis was reported as a serious adverse event for 12 participants, and numerically higher in the vaccine group, 8 vaccine participants and 4 placebo participants. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

on-Serious Adverse Events
In Study 2 in which 10,841 participants 16 through 55 years of age received Pfizer-BioNTech COVID-19 Vaccine and 10,851 participants received placebo, non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported in 29.3% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 13.2% of participants in the placebo group, for participants who received at least 1 dose. Overall in a similar analysis in which 7960 participants 56 years of age and older received Pfizer-BioNTech COVID-19 Vaccine, non-serious adverse events within 30 days were reported in 23.8% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 11.7% of participants in the placebo group, for participants who received at least 1 dose. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

The higher frequency of reported unsolicited non-serious adverse events among Pfizer-BioNTech COVID-19 Vaccine recipients compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following vaccination that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Tables 3 and 4. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy were imbalanced with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (64) vs. the placebo group (6), which is plausibly related to vaccination. Throughout the safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the Pfizer-BioNTech COVID-19 Vaccine group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of Bell's palsy were reported in the placebo group. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Adolescents 12 Through 1 ears of Age

In an analysis of Study 2, based on data up to the cutoff date of March 13, 2021, 2,260 adolescents (1,131 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA); 1,129 placebo) were 12 through 15 years of age. Of these, 1,308 (660 Pfizer-BioNTech COVID-19 Vaccine and 648 placebo) adolescents have been followed for at least 2 months after the second dose. The safety evaluation in Study 2 is ongoing.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among adolescents who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the adolescents who received the Pfizer-BioNTech COVID-19 Vaccine, 50.1% were male and 49.9% were female, 85.9% were White, 4.6% were Black or African American, 11.7% were Hispanic/Latino, 6.4% were Asian, and 0.4% were American Indian/Alaska Native.

Solicited ocal and Systemic Adverse Reactions

The mean duration of pain at the injection site after Dose 1 was 2.4 days (range 1 to 10 days), for redness 2.4 days (range 1 to 16 days), and for swelling 1.9 days (range 1 to 5 days) for adolescents in the Pfizer-BioNTech COVID-19 Vaccine group.

Table 5: Study 2 – Frequency and Percentages of Adolescents With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Adolescents 12 Through 15 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Redness[c]				
Any (>2 cm)	65 (5.8)	12 (1.1)	55 (5.0)	10 (0.9)
Mild	44 (3.9)	11 (1.0)	29 (2.6)	8 (0.7)
Moderate	20 (1.8)	1 (0.1)	26 (2.4)	2 (0.2)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling[c]				
Any (>2 cm)	78 (6.9)	11 (1.0)	54 (4.9)	6 (0.6)
Mild	55 (4.9)	9 (0.8)	36 (3.3)	4 (0.4)
Moderate	23 (2.0)	2 (0.2)	18 (1.6)	2 (0.2)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain at the injection site[d]				
Any	971 (86.2)	263 (23.3)	866 (78.9)	193 (17.9)
Mild	467 (41.4)	227 (20.1)	466 (42.5)	164 (15.2)
Moderate	493 (43.7)	36 (3.2)	393 (35.8)	29 (2.7)
Severe	11 (1.0)	0 (0.0)	7 (0.6)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 6: Study 2 – Frequency and Percentages of Adolescents with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Adolescents 12 Through 15 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Fever				
≥38.0℃	114 (10.1)	12 (1.1)	215 (19.6)	7 (0.6)
≥38.0℃ to 38.4℃	74 (6.6)	8 (0.7)	107 (9.8)	5 (0.5)
>38.4℃ to 38.9℃	29 (2.6)	2 (0.2)	83 (7.6)	1 (0.1)
>38.9℃ to 40.0℃	10 (0.9)	2 (0.2)	25 (2.3)	1 (0.1)
>40.0℃	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[c]				
Any	677 (60.1)	457 (40.6)	726 (66.2)	264 (24.5)
Mild	278 (24.7)	250 (22.2)	232 (21.1)	133 (12.3)
Moderate	384 (34.1)	199 (17.7)	468 (42.7)	127 (11.8)
Severe	15 (1.3)	8 (0.7)	26 (2.4)	4 (0.4)
Headache[c]				
Any	623 (55.3)	396 (35.1)	708 (64.5)	263 (24.4)
Mild	361 (32.0)	256 (22.7)	302 (27.5)	169 (15.7)
Moderate	251 (22.3)	131 (11.6)	384 (35.0)	93 (8.6)
Severe	11 (1.0)	9 (0.8)	22 (2.0)	1 (0.1)
Chills[c]				
Any	311 (27.6)	109 (9.7)	455 (41.5)	73 (6.8)
Mild	195 (17.3)	82 (7.3)	221 (20.1)	52 (4.8)
Moderate	111 (9.8)	25 (2.2)	214 (19.5)	21 (1.9)
Severe	5 (0.4)	2 (0.2)	20 (1.8)	0 (0.0)
Vomiting[d]				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Mild	30 (2.7)	8 (0.7)	25 (2.3)	11 (1.0)
Moderate	0 (0.0)	2 (0.2)	4 (0.4)	1 (0.1)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea[e]				
Any	90 (8.0)	82 (7.3)	65 (5.9)	43 (4.0)
Mild	77 (6.8)	72 (6.4)	59 (5.4)	38 (3.5)
Moderate	13 (1.2)	10 (0.9)	6 (0.5)	5 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain[c]				
Any	272 (24.1)	148 (13.1)	355 (32.4)	90 (8.3)
Mild	125 (11.1)	88 (7.8)	152 (13.9)	51 (4.7)
Moderate	145 (12.9)	60 (5.3)	197 (18.0)	37 (3.4)
Severe	2 (0.2)	0 (0.0)	6 (0.5)	2 (0.2)

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
New or worsened joint pain[c]				
Any	109 (9.7)	77 (6.8)	173 (15.8)	51 (4.7)
Mild	66 (5.9)	50 (4.4)	91 (8.3)	30 (2.8)
Moderate	42 (3.7)	27 (2.4)	78 (7.1)	21 (1.9)
Severe	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)
Use of antipyretic or pain medication[f]	413 (36.6)	111 (9.8)	557 (50.8)	95 (8.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.
a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

<u>*Unsolicited Adverse Events*</u>

In the following analyses of Study 2 in adolescents 12 through 15 years of age (1,131 of whom received Pfizer-BioNTech COVID-19 Vaccine and 1,129 of whom received placebo), 98.3% of study participants had at least 30 days of follow-up after Dose 2.

Serious Adverse Events
Serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.1% of placebo recipients. There were no notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

on-Serious Adverse Events
Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 5.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 5.8% of placebo recipients. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy plausibly related to the study intervention were imbalanced, with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (7) vs. the placebo group (1). There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

<u>Booster Dose Following a Primary Series of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY</u>

A subset of Study 2 Phase 2/3 participants of 306 adults 18 through 55 years of age received a booster dose of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) approximately 6 months (range of 4.8 to 8.0 months) after completing the primary series. Additionally, a total of 23 Study 2 Phase 1 participants (11 participants 18 through 55 years of age and 12 participants 65 through 85 years of age) received a booster dose of Pfizer-BioNTech COVID-19 Vaccine approximately 8 months (range 7.9 to 8.8 months) after completing the

primary series. Safety monitoring after the booster dose was the same as that in the reactogenicity subset who received the primary series.

Among the 306 Phase 2/3 participants, the median age was 42 years (range 19 through 55 years of age), 45.8% were male and 54.2% were female, 81.4% were White, 27.8% were Hispanic/Latino, 9.2% were Black or African American, 5.2% were Asian, and 0.7% were American Indian/Alaska Native. Among the 12 Phase 1 participants 65 through 85 years of age, the median age was 69 years (range 65 through 75 years of age), 6 were male and all were White and Not Hispanic/Latino. Following the booster dose, the median follow-up time was 2.6 months (range 2.1 to 2.9 months) for Phase 1 participants and 2.6 months (range 1.1 to 2.8 months) for Phase 2/3 participants.

Solicited ocal and Systemic Adverse Reactions

Table 7 and Table 8 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of a booster dose of Pfizer-BioNTech COVID-19 Vaccine for Phase 2/3 participants 18 through 55 years of age.

In participants who received a booster dose, the mean duration of pain at the injection site after the booster dose was 2.6 days (range 1 to 8 days), for redness 2.2 days (range 1 to 15 days), and for swelling 2.2 days (range 1 to 8 days).

Table 7: Study 2 – Frequency and Percentages of Participants With Solicited Local Reactions, By Maximum Severity, Within 7 Days After the Booster Dose of Pfizer-BioNTech COVID-19 Vaccine – Participants 18 through 55 Years of Age*

Solicited Local Reaction	**Pfizer-BioNTech COVID-19 Vaccine† Booster Dose N[a] = 289 n[b] (%)**
Redness[c]	
Any (>2 cm)	17 (5.9)
Mild	10 (3.5)
Moderate	7 (2.4)
Severe	0
Swelling[c]	
Any (>2 cm)	23 (8.0)
Mild	13 (4.5)
Moderate	9 (3.1)
Severe	1 (0.3)
Pain at the injection site[d]	
Any	240 (83.0)
Mild	174 (60.2)
Moderate	65 (22.5)
Severe	1 (0.3)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after the booster dose.
Note: No Grade 4 solicited local reactions were reported.
* A subset of Phase 2/3 participants 18 through 55 years of age who received a booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) approximately 6 months after completing the primary series.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to 5.0 cm; Moderate: >5.0 to 10.0 cm; Severe: >10.0 cm.

Solicited Local Reaction	Pfizer-BioNTech COVID-19 Vaccine† Booster Dose N[a] = 289 n[b] (%)

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 8: Study 2 – Frequency and Percentages of Participants With Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After the Booster Dose of Pfizer-BioNTech COVID-19 Vaccine – Participants 18 through 55 Years of Age*

Solicited Systemic Reaction	Pfizer-BioNTech COVID-19 Vaccine† Booster Dose N[a] = 289 n[b] (%)
Fever	
≥38.0℃	25 (8.7)
≥38.0℃ to 38.4℃	12 (4.2)
>38.4℃ to 38.9℃	12 (4.2)
>38.9℃ to 40.0℃	1 (0.3)
>40.0℃	0
Fatigue[c]	
Any	184 (63.7)
Mild	68 (23.5)
Moderate	103 (35.6)
Severe	13 (4.5)
Headache[c]	
Any	140 (48.4)
Mild	83 (28.7)
Moderate	54 (18.7)
Severe	3 (1.0)
Chills[c]	
Any	84 (29.1)
Mild	37 (12.8)
Moderate	44 (15.2)
Severe	3 (1.0)
Vomiting[d]	
Any	5 (1.7)
Mild	5 (1.7)
Moderate	0
Severe	0
Diarrhea[e]	
Any	25 (8.7)
Mild	21 (7.3)
Moderate	4 (1.4)
Severe	0

Solicited Systemic Reaction	Pfizer-BioNTech COVID-19 Vaccine† Booster Dose N[a] = 289 n[b] (%)
New or worsened muscle pain[c]	
Any	113 (39.1)
Mild	52 (18.0)
Moderate	57 (19.7)
Severe	4 (1.4)
New or worsened joint pain[c]	
Any	73 (25.3)
Mild	36 (12.5)
Moderate	36 (12.5)
Severe	1 (0.3)
Use of antipyretic or pain medication[f]	135 (46.7)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after the booster dose.
Note: No Grade 4 solicited systemic reactions were reported.
* A subset of Phase 2/3 participants 18 through 55 years of age who received a booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) approximately 6 months after completing the primary series.
† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).
a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

In Phase 1 participants ≥65 years of age (n = 12), local reaction pain at the injection site (n = 8, 66.7%) and systemic reactions fatigue (n = 5, 41.7%), headache (n = 5, 41.7%), chills (n = 2, 16.7%), muscle pain (n = 4, 33.3%), and joint pain (n = 2, 16.7%) were reported after the booster dose. No participant in this age group reported a severe systemic event or fever after the booster dose.

Unsolicited Adverse Events

Overall, the 306 participants who received a booster dose, had a median follow-up time of 2.6 months after the booster dose to the cut-off date (June 17, 2021).

In an analysis of all unsolicited adverse events reported following the booster dose, through 1 month after the booster dose, in participants 18 through 55 years of age (N = 306), those assessed as adverse reactions not already captured by solicited local and systemic reactions were lymphadenopathy (n = 16, 5.2%), nausea (n = 2, 0.7%), decreased appetite (n = 1, 0.3%), rash (n = 1, 0.3%), and pain in extremity (n = 1, 0.3%).

Serious Adverse Events

Of the 306 participants who received a booster dose of Pfizer-BioNTech COVID-19 Vaccine, there were no serious adverse events reported from the booster dose through 30 days after the booster dose. One participant reported a serious adverse event 61 days after the booster dose that was assessed as unrelated to vaccination.

Booster Dose Following Primary Vaccination with Another Authorized COVID-19 Vaccine

The safety of a Pfizer-BioNTech COVID-19 Vaccine booster dose (30 mcg modRNA) in individuals who completed primary vaccination with another authorized COVID-19 Vaccine (heterologous booster dose) is inferred from the safety of a Pfizer-BioNTech COVID-19 Vaccine booster dose administered following completion of Pfizer-BioNTech COVID-19 Vaccine primary series (homologous booster dose) and from data from an independent National Institutes of Health (NIH) study Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA). Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported in the study following the Pfizer-BioNTech COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following a Pfizer-BioNTech COVID-19 Vaccine primary series doses or homologous booster dose.

6.2 Post Authorization Experience

The following adverse reactions have been identified during post authorization use of Pfizer-BioNTech COVID-19 Vaccine. Because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)
Nervous System Disorders: syncope

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS[5]

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following Pfizer-BioNTech COVID-19 Vaccine to the Vaccine Adverse Event Reporting System (VAERS):

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome (MIS) in children and adults
- Cases of COVID-19 that result in hospitalization or death

[5] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

*Serious adverse events are defined as:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent 1 of the outcomes listed above

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using 1 of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of the Pfizer-BioNTech COVID-19 Vaccine
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on Pfizer-BioNTech COVID-19 Vaccine and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within 1 month prior.
2. In Box 18, description of the event:
    a. Write "Pfizer-BioNTech COVID-19 Vaccine EUA" as the first line.
    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.

c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

10 DRUG INTERACTIONS

There are no data to assess the concomitant administration of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (30 mcg) and other ingredients included in a single human dose of Pfizer-BioNTech COVID-19 Vaccine was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Pfizer-BioNTech COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Emergency Use Authorization of this formulation of Pfizer-BioNTech COVID-19 Vaccine, supplied in multiple dose vials with purple caps, in adolescents 12 through 17 years of age is based on safety and effectiveness data in this age group and in adults.

For individuals 5 through 11 years of age, a different formulation of the Pfizer-BioNTech COVID-19 Vaccine is authorized.

Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine does not include use in individuals younger than 5 years of age.

11.4 Geriatric Use

Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older who received the primary series and their data contributes to the overall assessment of safety and efficacy *[see Overall Safety Summary (6.1) and Clinical Trial Results and Supporting Data for EUA (18.1)]*. Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients in Study 2 (N=20,033), 21.4% (n=4,294) were 65 years of age and older and 4.3% (n=860) were 75 years of age and older.

The safety of a booster dose of Pfizer-BioNTech COVID-19 Vaccine in individuals 65 years of age and older is based on safety data in 12 booster dose recipients 65 through 85 years of age and 306 booster dose recipients 18 through 55 years of age in Study 2. The effectiveness of a booster dose of Pfizer-BioNTech COVID-19 Vaccine in individuals 65 years of age and older is based on effectiveness data in 306 booster dose recipients 18 through 55 years of age in Study 2.

11.5 Use in Immunocompromised

From an independent report *(amar Abravanel F arion O et al. Three doses of an mR A Covid-1 vaccine in solid-organ transplant recipients. Engl ed)*, safety and effectiveness of a third dose of the Pfizer-BioNTech COVID-19 vaccine have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

13 DESCRIPTION

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials with purple caps; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The

diluent (sterile 0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

The Pfizer-BioNTech COVID-19 Vaccine does not contain preservative. The vial stoppers are not made with natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The modRNA in the Pfizer-BioNTech COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Efficacy of Primary Series in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) or placebo separated by 21 days. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the Pfizer-BioNTech COVID-19 Vaccine group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 9 presents the specific demographic characteristics in the studied population.

Table 9: Demographics (population for the primary efficacy endpoint)[a]

	Pfizer-BioNTech COVID-19 Vaccine* (N=18,242) n (%)	Placebo (N=18,379) n (%)
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)

	Pfizer-BioNTech COVID-19 Vaccine* (N=18,242) n (%)	**Placebo (N=18,379) n (%)**
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years[b]	46 (0.3)	42 (0.2)
≥16 through 17 years	66 (0.4)	68 (0.4)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[c]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[d]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

* Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. 100 participants 12 through 15 years of age with limited follow-up in the randomized population received at least 1 dose (49 in the vaccine group and 51 in the placebo group). Some of these participants were included in the efficacy evaluation depending on the population analyzed. They contributed to exposure information but with no confirmed COVID-19 cases, and did not affect efficacy conclusions.

c. Includes multiracial and not reported.

d. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease
- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2 or gestational)
- Liver disease
- Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 10.

Table 10: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine† N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All subjects[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 through 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without evidence of prior SARS-CoV-2 infection			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine† N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
All subjects[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 through 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. No confirmed cases were identified in adolescents 12 through 15 years of age.
f. Credible interval for vaccine efficacy (VE) was calculated using a beta-binomial model with a beta (0.700102, 1) prior for θ=r(1-VE)/(1+r(1-VE)), where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.
g. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

18.2 Efficacy of Primary Series in Adolescents 12 Through 15 Years of Age

A descriptive efficacy analysis of Study 2 has been performed in approximately 2,200 adolescents 12 through 15 years of age evaluating confirmed COVID-19 cases accrued up to a data cutoff date of March 13, 2021.

The efficacy information in adolescents 12 through 15 years of age is presented in Table 11.

Table 11: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period, Adolescents 12 Through 15 Years of Age Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 through 15 years of age without evidence of prior SARS-CoV-2 infection*			
	Pfizer-BioNTech COVID-19 Vaccine† N[a]=1005 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=978 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
Adolescents 12 through 15 years of age	0 0.154 (1001)	16 0.147 (972)	100.0 (75.3, 100.0)
First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 through 15 years of age with or without evidence of prior SARS-CoV-2 infection			
	Pfizer-BioNTech COVID-19 Vaccine† N[a]=1119 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=1110 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
Adolescents 12 through 15 years of age	0 0.170 (1109)	18 0.163 (1094)	100.0 (78.1, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

18.3 Immunogenicity of Primary Series in Adolescents 12 Through 15 Years of Age

In Study 2, an analysis of SARS-CoV-2 50% neutralizing titers (NT50) 1 month after Dose 2 in a randomly selected subset of participants demonstrated non-inferior immune responses (within 1.5-fold) comparing adolescents 12 through 15 years of age to participants 16 through 25 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2 (Table 12).

Table 12: Summary of Geometric Mean Ratio for 50% Neutralizing Titer – Comparison of Adolescents 12 Through 15 Years of Age to Participants 16 Through 25 Years of Age (Immunogenicity Subset) –Participants Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine*		12 Through 15 Years/ 16 Through 25 Years	
		12 Through 15 Years n[a]=190	16 Through 25 Years n[a]=170		
Assay	Time Point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMR[d] (95% CI[d])	Met Noninferiority Objective[e] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[f]	1 month after Dose 2	1239.5 (1095.5, 1402.5)	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Y

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic-acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Participants who had no serological or virological evidence (up to 1 month after receipt of the last dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 were included in the analysis.

* Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.

b. Protocol-specified timing for blood sample collection.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1 [12 through 15 years of age] – Group 2 [16 through 25 years of age]) and the corresponding CI (based on the Student t distribution).

e. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

f. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

18.4 Immunogenicity of a Booster Dose Following a Pfizer-BioNTech COVID-19 Vaccine Primary Series in Participants 18 Through 55 Years of Age

Effectiveness of a booster dose of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) was based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). In Study 2, analyses of NT50 1 month after the booster dose compared to 1 month after the primary series in individuals 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination demonstrated noninferiority for both geometric mean ratio (GMR) and difference in seroresponse rates. Seroresponse for a participant was defined as achieving a ≥4-fold rise in NT50 from baseline (before primary series). These analyses are summarized in Table 13 and Table 14.

Table 13: Geometric Mean 50% Neutralizing Titer (SARS-CoV-2 USA_WA1/2020) – Comparison of 1 Month After Booster Dose to 1 Month After Primary Series – Participants 18 Through 55 Years of Age Without Evidence of Infection up to 1 Month After Booster Dose* – Booster Dose Evaluable Immunogenicity Population±

Assay	n[a]	1 Month After Booster Dose GMT[b] (95% CI[b])	1 Month After Primary Series GMT[b] (95% CI[b])	1 Month After Booster Dose/ 1 Month After Primary Series GMR[c] (97.5% CI[c])	Met Noninferiority Objective[d] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[e]	212	2466.0 (2202.6, 2760.8)	750.6 (656.2, 858.6)	3.29 (2.77, 3.90)	Y

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.

Note: Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

* Participants who had no serological or virological evidence (up to 1 month after receipt of a booster dose of Pfizer-BioNTech COVID-19 Vaccine) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose were included in the analysis.

± All eligible participants who had received 2 doses of Pfizer-BioNTech COVID-19 Vaccine as initially randomized, with Dose 2 received within the predefined window (within 19 to 42 days after Dose 1), received a booster dose of Pfizer-BioNTech COVID-19 Vaccine, had at least 1 valid and determinate immunogenicity result after booster dose from a blood collection within an appropriate window (within 28 to 42 days after the booster dose), and had no other important protocol deviations as determined by the clinician.

a. n = Number of participants with valid and determinate assay results at both sampling time points within specified window.

b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

c. GMRs and 2-sided 97.5% CIs were calculated by exponentiating the mean differences in the logarithms of the assay and the corresponding CIs (based on the Student t distribution).

d. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.80.

e. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Table 14: Seroresponse Rate for 50% Neutralizing Titer (SARS-CoV-2 USA_WA1/2020) – Comparison of 1 Month After Booster Dose to 1 Month After Primary Series – Participants 18 Through 55 Years of Age Without Evidence of Infection up to 1 Month After Booster Dose* – Booster Dose Evaluable Immunogenicity Population±

Assay	N[a]	1 Month After Booster Dose n[b] % (95% CI[c])	1 Month After Primary Series n[b] % (95% CI[c])	Difference (1 Month After Booster Dose - 1 Month After Primary Series) %[d] (97.5% CI[e])	Met Noninferiority Objective[f] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[g]	200	199 99.5 (97.2, 100.0)	196 98.0 (95.0, 99.5)	1.5 (-0.7, 3.7)	Y

Abbreviations: CI = confidence interval; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.

Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.

Note: Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

* Participants who had no serological or virological evidence (up to 1 month after receipt of booster vaccination) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after booster vaccination were included in the analysis.

± All eligible participants who had received 2 doses of Pfizer-BioNTech COVID-19 Vaccine as initially randomized, with Dose 2 received within the predefined window (within 19 to 42 days after Dose 1), received a booster dose of Pfizer-BioNTech COVID-19 Vaccine, had at least 1 valid and determinate immunogenicity result after booster dose from a blood collection within an appropriate window (within 28 to 42 days after the booster dose), and had no other important protocol deviations as determined by the clinician.

a. N = number of participants with valid and determinate assay results for the specified assay at baseline, 1 month after Dose 2 and 1 month after the booster dose within specified window. These values are the denominators for the percentage calculations.
b. n = Number of participants with seroresponse for the given assay at the given dose/sampling time point.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Difference in proportions, expressed as a percentage (1 month after booster dose – 1 month after Dose 2).
e. Adjusted Wald 2-sided CI for the difference in proportions, expressed as a percentage.
f. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the percentage difference is > -10%.
g. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

18.5 Immunogenicity in Solid Organ Transplant Recipients

From an independent report *(amar Abravanel F arion O et al. Three doses of an mR A Covid-1 vaccine in solid-organ transplant recipients. Engl ed)*, a single arm study has been conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of the Pfizer-BioNTech COVID-19 vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

18.6 Immunogenicity of a Booster Dose Following Primary Vaccination with Another Authorized COVID-19 Vaccine

Effectiveness of a Pfizer-BioNTech COVID-19 Vaccine booster dose (30 mcg modRNA) in individuals who completed primary vaccination with another authorized COVID-19 Vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Pfizer-BioNTech COVID-19 Vaccine booster dose administered following completion of Pfizer-BioNTech COVID-19 Vaccine primary series and from immunogenicity data from an independent NIH study Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA). Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Pfizer-BioNTech COVID-19 Vaccine was demonstrated regardless of primary vaccination.

19 HOW SUPPLIED/STORAGE AND HANDLING

The information in this section applies to the Pfizer-BioNTech COVID-19 Vaccine that is supplied in multiple dose vials with a purple cap. These multiple dose vials are supplied in a carton containing 25 multiple dose vials (NDC 59267-1000-3) or 195 multiple dose vials (NDC 59267-1000-2). After dilution, 1 vial contains 6 doses of 0.3 mL. Vial labels and cartons may state that after dilution, a vial contains 5 doses of 0.3 mL. The information in this Full EUA Prescribing Information regarding the number of doses per vial after dilution supersedes the number of doses stated on vial labels and cartons.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with purple caps arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. This information in the package insert supersedes the storage conditions printed on the vial cartons.

Cartons and vials of Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps with an expiry date of July 2021 through February 2022 printed on the label may remain in use for 3 months beyond the printed date as long as approved storage conditions between -90ºC to -60ºC (-130ºF to -76ºF) have been maintained. Updated expiry dates are shown below.

Printed Expiry Date		Updated Expiry Date
July 2021	→	October 2021
August 2021	→	November 2021
September 2021	→	December 2021
October 2021	→	January 2022
November 2021	→	February 2022
December 2021	→	March 2022
January 2022	→	April 2022
February 2022	→	May 2022

If not stored between -90ºC to -60ºC (-130ºF to -76ºF), vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Tha ed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Tha ed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Vaccine Information Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at: https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

This Full EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please see www.cvdvaccine.com.

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